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MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

10/11/2016

MODULE 1

PRODUCT SUMMARY

EU Procedure number	FR/V/0238/001/MR
Name, strength and pharmaceutical form	Cevac Landavax SC Emulsion for injection
Applicant	CEVA SANTE ANIMALE
Active substance(s)	*Pasteurella multocida*, strain X73 (serovar A1) *Pasteurella multocida*, strain P-1059 (serovar A3)
ATC Vetcode	QI01BB
Target species	Ducks
Indication for use	Active immunisation in order to reduce mortality, morbidity and clinical signs associated with infection caused by *Pasteurella multocida* capsule type A, serovars 1 and 3

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	21/03/2012
Date product first authorised in the Reference Member State (MRP only)	15/10/2010
Concerned Member States for original procedure	BG, HU

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:

ingredients	Quantity per dose (0.5 ml)
Active ingredients *Pasteurella multocida* strain X-73, A1 serotype *Pasteurella multocida* strain P-1059, A3 serotype	 at least 80% of protection in susceptible chicken at least 65% of protection in susceptible turkeys
Adjuvant(s) Oil adjuvant	 0.300 ml
Excipient(s) Paraffin light liquid, Sorbitan oleate, Polysorbate 80, Thiomersal, Sodium chloride, disodium phosphate dehydrate, potassium phosphate, water for injection	

The vials (50 or 500 ml) are of low density polyethylene (LDPE) that comply with Eur. Ph. 3.1.4, closed with nitrile stoppers (Eur. Ph. 3.2.9) and sealed with an aluminium cap. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the adjuvant (oil adjuvant), vaccine strains (*Pasteurella multocida* strain X-73, A1 serotype and strain P-1059, A3 serotype), formulation, inactivating agent (formaldehyde), presence of preservative (thiomersal) are justified.

The inactivation process and the detection limit of the control of inactivation are correctly validated.

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 is *Pasteurella multocida*, a novel active substance. The active substance is manufactured in accordance with the principles of good manufacturing practice.

Starting materials of non-biological origin used in production comply with pharmacopoeia monographs 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; 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: appearance, free formaldehyde content, thiomersal content, viscosity, type and stability of emulsion, potency test for A1 and A3 components, sterility test, TABST. The inactivation test is performed immediately after inactivation and not repeated on the bulk vaccine.
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 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 when stored under the approved conditions.

The in-use shelf-life of the broached vaccine is supported by the data provided.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

This vaccine falls within the scope of the EMA guideline EMA/CVMP/IWP/123243/2006 for vaccines intended for “minor use or minor species / limited markets”. The assessment has been made taking this guideline into consideration.

III. SAFETY ASSESSMENT

The studies were performed with batch 0103RBPK, standard formulation.

Laboratory trials

The safety of the administration of one dose, an overdose and the repeated administration of one dose in the target animal is demonstrated in a study involving 3 groups of 29 ducks, including a control group. The investigation was performed according to the recommendations of Directive 2001/82/EC as amended and the relevant guidelines and of the Ph. Eur. Monograph 1945 (fowl cholera inactivated vaccine). The SPC describes the frequency and size of local reactions observed.

No investigation of effect on reproductive performance was conducted because the vaccine is not intended for this category of animals.

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 compounds present in the final vaccine formulation:

- light liquid paraffin
- sorbitan oleate
- polysorbate 80
- thiomersal – less than 0.02% in the final product.

All these 4 compounds are in Annex II of Council regulation 2377/90, there is no need to carry out study for residues. 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

A field study involving 2 different farms included 2800 birds vaccinated with Cevac Landavax, as well as birds vaccinated with a competitor vaccine and sentinels (unvaccinated birds). Local reactions were observed as during the

laboratory study, as well as a transcient post-vaccination apathy. These adverse effects are reported in the SPC.

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 required.
This is a vaccine containing an oil adjuvant which may induce severe local reaction if self-injected. The appropriate warning for the user is included in the SPC.

IV. CLINICAL ASSESSMENT (EFFICACY)

IV.B Clinical Studies (pharmaceuticals and immunologicals)

Laboratory Trials

The efficacy of the product has been demonstrated in 10 laboratory studies involving 400 ducks vaccinated with Cevac Landavax, as well as controls ducks and chicken and turkeys (to validate the batch potency tests) in accordance with the relevant requirements. They showed that :

- Regarding the minimum age at vaccination, the efficacy according to Ph. Eur. monograph 1945 is established for both components by an heterologous challenge in seronegative mullard duck.
- Regarding the onset of immunity, the efficacy according to Ph. Eur. monograph 1945 is established for both components by an heterologous challenge in seronegative mullard duck.
- Regarding the duration of immunity, the efficacy is established by an heterologous challenge for the A3 component and by an homologous challenge for the A1 component in seronegative mullard duck. However, in the onset of immunity studies, the vaccine gave the same level of protection following an heterologous and an homologous challenge; thus, an homologous challenge to establish the duration of immunity is acceptable.
- Regarding the indication, the reduction in mortality and morbidity was not statistically established (no statistical analysis planed). However, as far as the results are conform to the Ph. Eur. monograph 1945 which is based on the analysis of the morbidity and mortality, this claim of reduction of mortality and morbidity is accepted.
- Regarding the effect of maternally derived antibodies : serology performed in 3-week-old mallard ducks confirmed that both in France and Hungary the ducks had no more detectable MDA at this age. The

indication for use from the age of 3 weeks is thus acceptable, but a warning is given in the SPC regarding the lack of information on the possible interferences from the presence of maternal antibodies on the response to vaccination

Field Trials

A field study has been conducted in France. There was however no exposure to a natural challenge during the course of the trial, therefore, there are no field efficacy data. This is acceptable as field trials are not required for MUMS products provided the laboratory data have clearly established the efficacy of the product, according to the MUMS Guideline EMEA/CVMP/IWP/123243/2006 which states that “if sufficient laboratory studies show efficacy then field studies are 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 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://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**
Secondary packaging site	2012
Additional quality control test site	2013
Increase in bacterial endotoxin limits in the final product	2014
Increase in bacterial count of *Pasteurella multocida* A1 before inactivation	2015