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DEPARTAMENTO DE
MEDICAMENTOS
VETERINARIOS

Agencia Española de Medicamentos y Productos Sanitarios

C/Campezo 1, Edificio 8
28022 – Madrid
España
(Reference Member State)

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

ALPHA DIP Vib concentrate for dip suspension for sea bass

CORREO ELECTRÓNICO

mresvet@aemps.es

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C/ CAMPEZO, 1 – EDIFICIO 8
28022 MADRID
TEL: 91 822 54 01
FAX: 91 822 5443

MODULE 1

PRODUCT SUMMARY

EU Procedure number	ES/V/0251/001/DC
Name, strength and pharmaceutical form	ALPHA DIP Vib concentrate for dip suspension for sea bass.
Applicant	PHARMAQ AS Industrivegen 50 7863 Overhalla (Norway)
Active substance(s)	VIBRIO (LISTONELLA) ANGUILLARUM, INACTIVADA, SEROTIPO O1, CEPA AL 112
ATC Vet code	QI10X
Target species	Sea bass (<i>Dicentrarchus labrax</i>)
Indication for use	For active immunisation of sea bass to reduce mortality and clinical signs caused by infection with <i>Listonella anguillarum</i> serotype O1 (vibriosis).



MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies website (<http://www.hma.eu>).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Decentralised application in accordance with Article 12.3 of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	D210= 24.02.2016
Date product first authorised in the Reference Member State (MRP only)	N/A
Concerned Member States for original procedure	EL, HR, IT and PT

I. SCIENTIFIC OVERVIEW

For public assessment reports for the first authorisation in a range:

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 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 *Listonella anguillarum* (*Vibrio anguillarum*) serotype O1, strain AL 112 and as excipients purified water (the vaccine may contain formaldehyde as a residue after inactivation).

The containers are sterile transparent 500 ml or 1000 ml polyethylene terephthalate (PET) bottles with screw cap. The cap is of high density polyethylene (HDPE). The container is tamper-evident.

The container consists of two components, bottle and cap. The cap is available with and without a tamper evident tear-off ring. If the cap without a tear-off ring is used, a tamper evident plastic film will be applied over the cap and bottle during manufacturing.



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

The choice of the vaccine strain and formulation as well as the absence of preservative are 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 is the inactivated *Listonella anguillarum* serotype O1 antigen. The active substance is manufactured in accordance with the principles of good manufacturing practice.

The active substance specification is considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided.

Starting materials of non-biological origin used in production comply with pharmacopoeia monographs.

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

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

However, dossier includes risk assessment on the seed *L.anguillarum*, one starting material of animal origin but it is concluded that there is not potential risk of transmission of TSEs.

E. Control tests during production (immunologicals)

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 general characteristics of the product (appearance, free formaldehyde), identity of the active substance, potency, and sterility.

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 substance 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.

After dilution or reconstitution according to directions the vaccine should be used immediately

H. Genetically Modified Organisms

Non applicable.

J. Other Information

Non applicable.

III. SAFETY ASSESSMENT

ALPHA DIP Vib is an inactivated vaccine for sea bass against vibriosis. It is intended to protect juveniles in the early on-growing phase of the production cycle (from 1 gram) up to approximately 15 grams. Along the dossier, the applicant states that fish, at 15 grams will be vaccinated by an injectable oil adjuvanted vaccine. It has been demonstrated that the basic vaccination scheme is safe for fish used in the trial.

This vaccine is within the scope of the current MUMS guideline (EMA/CVMP/IWP/123243/2006-Rev.2) at day of submission. The laboratory trials have been performed in Sea bass of the recommended weight at vaccination.

The holder has assumed a commitment to provide data from field as a post approval vaccination. The follow up will be performed under commercial conditions until 21 days post second dip vaccination.

Laboratory trials

The applicant has presented two studies about an overdose administration and safety of the repeated administration of one dose. This in line with Directive 9/2009/EC and MUMS Guideline.

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 vaccine does not contain excipients other than purified water. The vaccine may contain formaldehyde as a residue after inactivation and it is stated in the SPC. 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.

Special precautions for use in animals and to be taken by the person administering the vaccine to the animals are also included in the SPC. Adverse reactions are not known

The following table shows a summary of the laboratory trials provided in the dossier:

Study	Type of study	Nº of fish	Results
Safety of an overdose	Observation of mortality and local and systemic reactions	250	The vaccine is safe for fish of 1 gram
Safety of an overdose	Observation of mortality and local and systemic reactions	100	The vaccine is safe for fish of 1 gram
Safety of a dose	Efficacy study but safety was	420	The vaccine is safe



according to the recommended schedule	also reported. Observation of mortality and behaviour		according to the recommended schedule.
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Field studies

According to MUMS Guideline, if laboratory studies sufficiently show no safety risk, field studies are not required. It should be sufficiently justified that data from the laboratory studies are representative for safety under field conditions. Safety data from the field may be required as a follow-up measure.

The assessment of laboratory studies justifies the absence of field studies.

Ecotoxicity

Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

IV. EFFICACY

ALPHA DIP Vib is an inactivated vaccine for sea bass against vibriosis. It is intended to protect juveniles in the early on-growing phase of the production cycle up to approximately 15 grams. At 15 grams, the fish are re-vaccinated by an injectable oil based vaccine.

ALPHA DIP Vib is claimed for active immunisation of sea bass to reduce mortality and clinical signs caused by infection with *Listonella anguillarum* serotype O1. The onset of immunity occurs no later than 600 degree days post vaccination.

IV.B Clinical Studies

The efficacy of the vaccine has been demonstrated in laboratory studies in accordance with the relevant requirements which show that the vaccine reduce mortality and clinical signs caused by infection with *Listonella anguillarum*) serotype O1 (vibriosis).

Onset of immunity is established at 600 degree days and duration of immunity has not been established. It is stated in section 4.2 of the SPC. However, the applicant accepts to provide efficacy data from the field as a post approval commitment. The follow-up will be performed under commercial conditions.

Laboratory trials:

The laboratory trials have been performed in Sea bass of the recommended weight at vaccination. A preliminary study to investigate the suitable challenge dose was carried out using unvaccinated fish.

The following table shows a summary of the laboratory trials provided in the dossier:

Study	Type of study	Nº of fish	Results
Efficacy of one dose	Challenge by intraperitoneal route 4 weeks after the vaccination	240	Fish vaccinated at 9.6 grams were protected
Efficacy according to the recommended schedule	Challenge by intraperitoneal route 4 and 5 weeks after the second dose	420	Fish vaccinated according to the recommended schedule were protected
Efficacy according to the recommended schedule	Challenge by intraperitoneal route 4 weeks after the second dose	300	Fish vaccinated according to the recommended schedule were protected

Field Trials

According to MUMS Guideline, if sufficient laboratory studies are performed, 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 (www.hma.eu).

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.

Administrative changes

Summary of change (Application number)	Section updated in Module 3	Approval date
ES/V/0251/001/II/001: Additional batch potency test site for ALPHA DIP Vib concentrate for dip suspension for the target species sea bass.	II	27.11.2016