FRENCH AGENCY FOR VETERINARY MEDICINAL PRODUCTS
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" DECENTRALISED" PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

MODULE 1

PRODUCT SUMMARY

EU Procedure number	FR/V/0349/002/DX/001
Name, strength and pharmaceutical form	ICTHIOVAC VNN, emulsion for injection for sea bass
Applicant	Laboratorios Hipra, S.A.
Active substance(s)	Inactivated Betanodavirus strain 1103
ATC Vetcode	QI10X
Target species	Sea bass (*Dicentrarchus labrax*)
Indication for use	For the active immunisation of sea bass to reduce the mortality caused by Viral Nervous Necrosis following infection by *Betanodavirus*. Onset of immunity: 42 days after vaccination at 22 ºC (924 degree days). Duration of immunity: 18 months.

MODULE 2

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

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Extension application in accordance with Article 12(3) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	21/09/2022
Date product first authorised in the Reference Member State (MRP only)	na
Concerned Member States for original procedure	CY, EL, ES, HR, IT, PT

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 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 product has been granted with a MUMS (Minor Use/Minor species) status.
The overall risk/benefit analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Composition

The product contains inactivated *Betanodavirus* strain 1103 (RP*[1] ≥ 1.3) and excipients (Montanide as adjuvant, sodium methyl parahydroxybenzoate and sodium propyl parahydroxybenzoate as preservative agents and disodium phosphate dodecahydrate, potassium dihydrogen phosphate, sodium chloride, potassium chloride and water for injections).

[1] RP : relative potency determined by ELISA, using a reference vaccine demonstrated to be efficacious

The container/closure system consists of 500 mL (5000 doses) high density polyethylene bottles and type I tuber stopper with aluminium cap. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the adjuvant, vaccine strain, formulation, inactivating agent and presence of preservatives 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 and in accordance with the European Pharmacopoeia and relevant European guidelines.

C. Control of Starting Materials

Starting materials of non-biological origin used in production comply with indicate 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 and European Guidelines.

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 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 in particular appearance, sodium methyl parahydroxybenzoate content, sodium propyl parahydroxybenzoate content, residual formaldehyde, Montanide content, antigen identification, potency test, viscosity, emulsion stability, sterility and volume control.
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 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 opened vaccine is supported by the data provided.

III. SAFETY ASSESSMENT

Vaccine batch used to perform the trials was a standard batch since the medicinal product is an inactivated vaccine authorised under MUMS status.

Laboratory trials

The safety of the administration of one dose, in the target animal is demonstrated in a study which involved 50 vaccinated fishes and 50 control fishes weighting at least 12.79g. They were kept in 100 L tanks in groups of 25.

They were vaccinated by intraperitoneal injection and followed after vaccination for 21 days and observed daily for local and systemic reactions, using a scoring system. At the end of the study, they were post-mortem examined to investigate pigmentation and adhesions and evaluate the presence or absence of vesicles (using a scoring system).

Results of the trial showed that the vaccine is safe for vaccinated fishes but adhesions and vesicles were observed. They resolved spontaneously.

The investigation was performed according to the recommendations of Directive 2001/82/EC as amended and the relevant guidelines.
Slight adhesions and vesicles of encapsulated vaccine are observed which are reported into the SPC as adverse events.
Additional support of the safety profile of the vaccine was given by follow-up of the fishes during the efficacy trials.

No investigation of effect on reproductive performance was conducted because the vaccine is not intended for breeders 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 adjuvant and excipients used are either allowed substances for which table 1 of the annex to the Commission Regulation (EU) No 37/2010 indicates that no MRLs are required or are considered as not falling within the scope of Regulation (EC) No. 470/2009 when used as in this veterinary medicinal product.

No specific assessment of the interaction of this product with other medicinal product was made. Therefore, an appropriate warning in the SPC is included.

The vaccine is safe for the user when used as recommended.

Field studies

No data from field study is available since the vaccine is authorised under MUMS status.

Ecotoxicity

The applicant provided a first phase 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.

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 support the indications of the vaccine as stated in the SPC including onset and duration of immunity.

Vaccine batches used to perform the trials were manufactured as described in the dossier.

First study :
Group of 50 fishes weighting at least 11.82 g were either vaccinated with a standard batch or with a minimum protective dose batch. Fishes were kept unvaccinated as control group.
They were reared at a temperature of 22+/-1°C at time of vaccination and at 26+/-1°C at time of challenge.
42 days after vaccination, 30 vaccinated fishes per group and 25 control fishes were challenged with a Betanodavirus challenge strain by intramuscular route.
After challenge, the fishes were monitored for clinical signs and mortality and a relative percentage of survival was calculated.
Results were showing that the mortality was above 60% in the control group and only 26.7% in the group vaccinated with the standard batch and 33.3% in the group vaccinated with the minimum protective dose batch. The relative percentages of survival were 72.2 and 65.3 respectively.
The study supported the onset of immunity as claimed in the SPC.

Second study :
Group of 60 fishes weighting approximatively 15 g and reared in four tanks were either vaccinated with a standard batch (standard formulation batch). Fishes were kept unvaccinated as control group.
They were reared at a temperature of 15-25°C at time of vaccination and at 26+/-1°C at time of challenge.
18 months after vaccination, the fishes were challenged with a Betanodavirus challenge strain by intramuscular route.
After challenge, the fishes were monitored for clinical signs and mortality and a relative percentage of survival was calculated.
Results were showing that the mortality reached 86.7% in the control group at the 6th day whereas the percentage of mortality in the vaccinated group was 23.3 (i.e a RPS of 73.1%) when considering the 4 tanks and 15.6 (i.e a RPS of 82.1%) when considering the three similar tanks (the fourth one showing a different behaviour).
The study supported the duration of immunity as claimed in the SPC.

Field Trials

No data from field study is available since the vaccine is authorised under MUMS status.

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.HEVRA.org).

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.

None