



**Veterinary
Medicines
Directorate**

**United Kingdom
Veterinary Medicines Directorate
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DECENTRALISED PROCEDURE

**PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY
MEDICINAL PRODUCT**

**ALPHA JECT micro 1 PD Emulsion for Injection, Vaccine for Atlantic
Salmon**

Date Created: 9th February 2016

**PuAR correct as of 14/09/2018 when RMS was transferred to FR. Please
contact the RMS for future updates.**

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0556/001/DC
Name, strength and pharmaceutical form	ALPHA JECT micro 1 PD Emulsion for Injection, Vaccine for Atlantic Salmon
Applicant	Pharmaq AS Skogmo Industriområde Industrivegen 50 7863 Overhalla Norway
Active substance(s)	Formaldehyde inactivated culture of: Salmon Pancreas Disease Virus (SPDV) strain AL V405 $RPS_{end}^a \geq 80\%$ ^a RPS_{end} = Relative percentage survival at end control mortality in a laboratory test in Atlantic salmon
ATC Vetcode	QI10AA 01
Target species	Atlantic salmon (<i>Salmo salar</i> L) with a minimum weight of 28 g
Indication for use	For active immunization of Atlantic salmon to reduce mortality, lesions in the heart and pancreas, and impaired growth caused by Pancreas Disease (PD). Onset of immunity occurs no later than 516 degree days after vaccination. Duration of immunity: The vaccine reduces mortality, lesions in the heart and pancreas and impaired growth caused by SPDV infection for up to at least 12 months after vaccination

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Product Information Database of the Veterinary Medicines Directorate.

www.gov.uk/check-animal-medicine-licensed

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	21 st October 2015
Date product first authorised in the Reference Member State (MRP only)	Not applicable
Concerned Member States for original procedure	Ireland Norway

I. SCIENTIFIC OVERVIEW

ALPHA JECT Micro 1 PD emulsion for injection, vaccine for Atlantic salmon is an inactivated, adjuvanted vaccine for the active immunisation of Atlantic salmon to reduce mortality, lesions in the heart and pancreas, and impaired growth caused by Pancreas Disease (PD). The product contains a formaldehyde-inactivated culture containing $RPS_{end}^1 \geq 80\%$ of Salmon Pancreas Disease Virus (SPDV) strain AL V405. The onset of immunity occurs no later than 516 degree days after vaccination. The vaccine reduces mortality, lesions in the heart and pancreas and impaired growth caused by SPDV infection for up to at least 12 months after vaccination. SPDV is included in the list of vaccines considered as minor use / limited markets (MUMS) in the CVMP "Guideline on data requirements for immunological veterinary medicinal products intended for minor use or minor species / limited markets". All data submitted for this application were deemed suitable for a MUMS application.

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, any reactions observed are indicated in the SPC². 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 efficacy³ of the product was demonstrated according to the claims made in the SPC.

The overall benefit/risk analysis is in favour of granting a marketing authorisation.

¹ RPS_{end} – Relative percentage survival at end control mortality in a laboratory test in Atlantic salmon.

² SPC – Summary of Product Characteristics.

³ Efficacy – The production of a desired or intended result.

II. QUALITY ASPECTS

II.A. Composition

The product contains a formaldehyde-inactivated culture of salmon PD virus strain AL V405 with a potency of $\geq 80\%$ relative percentage survival (RPS_{end}). It also contains the excipients liquid paraffin as an adjuvant, sorbitan oleate and polysorbate 80.

The container/closure system consists of 250 ml and 500 ml injection bags made of multilayer plastic foil with a rubber stopper closing the giving port. The particulars of the containers and controls performed are provided and conform to the regulation. The choice of the adjuvant, vaccine strain, inactivating agent and 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.

II.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. The manufacturing method consists of cell and virus propagation, purification, inactivation, concentration, diafiltration and subsequent blending, emulsification and filling into packs.

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

II.C. Control of Starting Materials

The active substance is SPDV. The active substance is manufactured in accordance with the principles of good manufacturing practice. Starting materials used in the product comply with the relevant Ph. Eur monographs.

Starting materials of non-biological origin used in production comply with 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 relevant guidelines. 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.

II.C.4. Substances of Biological Origin

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.

II.D. Control Tests Carried Out at Intermediate Stages of the Manufacturing Process

The tests performed during production are described and a suitable number conforming to the specifications, are provided. These tests include those for morphology and confluency of cell cultures, cytopathic effect, culture methodology, sterility, titration, inactivation, free formaldehyde analysis and concentration of virus.

II.E. 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 those for appearance, centrifugation, viscosity, free formaldehyde, potency of inactivated SPDV, sterility and purity.

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. Other supportive data provided confirm the consistency of the production process.

II.F. Stability

Stability data on the finished product have been provided in accordance with applicable European guidelines, demonstrating the stability of the product over a 15 month shelf life when stored at 2-8°C.

The in-use shelf-life of the vaccine after first opening the immediate packaging vaccine is 10 hours as supported by the data provided.

G. Other Information

Shelf life of the veterinary medicinal product as packaged for sale: 2 years

Shelf life after first opening the immediate packaging: 10 hours

Store and transport refrigerated (2 °C – 8 °C).

Do not freeze.

Protect from light.

III. SAFETY ASSESSMENT

Four laboratory studies and one field trial in support of the safety of the vaccine were provided. Safety criteria were tested in accordance with Ph. Eur. monograph 5.2.6 and the EMA⁴ guideline on the design of studies to evaluate the safety of fish vaccine.

Laboratory trials

A GLP safety study was performed to examine the safety of administration of one dose of the vaccine. The vaccine was administered at the recommended dose to fish smaller than the minimum weight recommended of 28 g. Fish were observed daily for signs of abnormal behaviour and for local adverse reactions, (scores, adhesions). No abnormal behaviours or reactions occurred during the 21 day observation period and no mortalities were recorded. Local reactions were mild to moderate, and only small amounts of vaccine residue were observed.

Two non GLP⁵-compliant safety studies were also performed to examine the safety of administration of one dose of the vaccine. The vaccine was administered at the recommended dose outlined in the SPC, to fish close to the minimum weight of 28 g. In these studies, fish were kept at conditions to promote side effects and observed appropriately. Mild to moderate intraperitoneal adhesions and pigmentation post vaccination were observed. No other abnormal behaviour or mortality was observed in any of the groups after vaccination, or during the study periods.

Although no longer a requirement for inactivated vaccines, the safety of an overdose was investigated in five studies. In each study fish Atlantic salmon were injected with twice the recommended dose of the vaccine and observed daily for 21 days. Any local reactions observed were mild to moderate.

No laboratory studies on the safety of the vaccine of the repeated administration of one dose were performed, as the product is only intended for administration by a single dose.

No investigation of the effect on reproductive performance was performed. A suitable warning is added to the SPC at Section 4.7. No investigation was performed with regard to immunological function, as vaccinated fish are not expected to be more susceptible to natural disease than unvaccinated fish. The vaccine is inactivated and thus the specific tests to be performed for live vaccines are not applicable. The withdrawal period is zero degree days as no Maximum Residue Limit is required for this type of product. Small oil deposits may be observed, but these are not seen in edible parts of the fish.

Five studies were performed which evaluated the proposed product administered simultaneously with other products. The SPC states:

⁴ EMA – European Medicines Agency.

⁵ GLP – Good Laboratory Practice.

- Safety and efficacy data are available which demonstrate that this vaccine can be administered simultaneously with PHARMAQ's oil adjuvanted multivalent vaccines containing the following antigens: *Aeromonas salmonicida*, *Listonella anguillarum* O1 and O2a, *Vibrio salmonicida*, *Moritella viscosa* and Infectious Pancreas Necrosis Virus (IPNV). The vaccines are administered intraperitoneally either simultaneously (one injection) or in immediate succession (two injections) while fish are anaesthetised.
- No information is available on the safety and efficacy of this vaccine when used with any other veterinary medicinal product except the products mentioned above. A decision to use this vaccine before or after any other veterinary medicinal product therefore needs to be made on a case by case basis.

Field studies

Because PD is regarded as MUMS, there was no need to perform field studies. However, in field studies performed by the applicant, results regarding local reactions from laboratory trials were confirmed.

User Safety

Proper precautions should be taken when vaccinating fish. The SPC and product literature carry suitable warnings with regard to accidental self-injection.

Ecotoxicity

The applicant provided a Phase 1 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)

Clinical Studies

Laboratory Trials

Eleven laboratory studies were carried out. The data were supported by efficacy results from three sites in a single field trial under natural challenge from PD.

Efficacy of a single dose of vaccine and onset of immunity

Three studies showed that a vaccine formula containing $RPS_{end} \geq 80\%$ of SPDV greatly reduced, or prevented mortality following challenge with SAV 3. Study 1 included fish of less than the proposed minimum age, (weighing 25 grams). Onset of immunity was proposed by the applicant as being 546 degree days on the basis of Study 4. However, in this study, the vaccine was not used at minimum potency. Based on Study 1, the onset of immunity was agreed as being 516 degree days.

A claim was also made for an indication for the reduction of lesions in the pancreas and heart, along with impaired growth, caused by PD. Suitable data were received in order to justify this claim. Vaccine batches used in relevant studies were higher than the minimum potency proposed; however, there is no requirement to use batches of vaccine in tests at minimum antigen level for vaccines classified as MUMS. Potency data were sufficient to support the claims of the product.

In the SPC, the duration of immunity is described as follows:

- The vaccine reduces mortality, lesions in the heart and pancreas and impaired growth caused by SPDV infection for up to at least 12 months after vaccination.

The product can be used simultaneously with PHARMAQ's oil adjuvanted multivalent vaccines containing: *Aeromonas salmonicida*, *Listonella anguillarum* O1 and O2a, *Vibrio salmonicida*, *Moritella viscosa* and Infectious Pancreas Necrosis Virus (IPNV). A decision to use the proposed vaccine before or after any other product must be made on a case by case basis by the responsible veterinarian.

Field Trials

There was no requirement to conduct field trials for this MUMS application. However, reduction of mortality during clinical outbreaks of Pancreas Disease has been documented up to 15 months post vaccination under field conditions.

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 benefit/risk profile of the product(s) is favourable.

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 Product Information Database of the Veterinary Medicines Directorate website.

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The post-authorisation assessment (PAA) 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.

The PAA for this product is available on the Product Information Database of the Veterinary Medicines Directorate website.

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