



**Veterinary
Medicines
Directorate**

**United Kingdom
Veterinary Medicines Directorate
Woodham Lane
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NATIONAL PROCEDURE

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

Aquavac 6 Emulsion for Injection for Atlantic Salmon

Date Created: November 2022

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Aquavac 6 Emulsion for Injection for Atlantic Salmon, Emulsion for injection
Applicant	MSD Animal Health UK Limited Walton Manor Walton Milton Keynes Buckinghamshire MK7 7AJ
Active substance(s)	Infectious pancreatic necrosis virus (IPNV) serotype Sp, inactivated, ≥ 1.5 ELISA units <i>Aeromonas salmonicida</i> subs. <i>salmonicida</i> , inactivated $\geq 10.7 \log_2$ ELISA units <i>Vibrio salmonicida</i> , inactivated, $\geq 90\%$ RPS <i>Vibrio anguillarum</i> serotype O1, inactivated $\geq 75\%$ RPS <i>Vibrio anguillarum</i> serotype O2a, inactivated $\geq 75\%$ RPS <i>Moritella viscosa</i> , inactivated $\geq 5.8 \log_2$ ELISA units
ATC Vetcode	QI10AL02
Target species	Salmon (Atlantic)
Indication for use	For active immunisation of Atlantic salmon to reduce clinical signs and mortality from infections with IPNV (Infectious pancreatic necrosis), <i>Aeromonas salmonicida</i> subsp. <i>salmonicida</i> (furunculosis), <i>Vibrio salmonicida</i> (cold-water vibriosis), <i>Vibrio anguillarum</i> serotype O1 and O2a (vibriosis), and <i>Moritella viscosa</i> (wound disease). Onset of immunity: 500 degree days after vaccination for the bacterial antigens and 608 degree days after vaccination for IPNV. Duration of immunity: at least 18 months for all bacterial antigens. Duration of immunity for IPNV has not been documented.

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 conclusion of the procedure	8/8/2022

I. SCIENTIFIC OVERVIEW

This was a full application in accordance with Article 12(3) of Directive 2001/82/EC as amended.

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 SPC.¹ 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 efficacy² 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.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains the inactivated active substances (antigens) *Aeromonas salmonicida* subsp. *salmonicida*, *Vibrio salmonicida*, *Listonella (Vibrio) anguillarum* serotype O1, *Listonella (Vibrio) anguillarum* serotype O2a, *Moritella viscosa* and IPNV. and the excipients light liquid paraffin, polysorbate 80, sorbitan monooleate, sodium chloride, potassium chloride, disodium phosphate dihydrate, potassium dihydrogen phosphate and water for injections.

The container/closure system consists of polyethylene terephthalate (PET) containers which are closed with rubber stoppers and sealed with aluminium caps. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the adjuvant and vaccine strain are justified.

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

¹ SPC – Summary of product Characteristics.

² Efficacy – The production of a desired or intended result.

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: scale up of working seed, inoculation, cultivation, harvest, inactivation, filtration, blending and homogenisation.

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

II.C. Control of Starting Materials

The active substances are inactivated (antigens) *Aeromonas salmonicida* subsp. *salmonicida*, *Vibrio salmonicida*, *Listonella (Vibrio) anguillarum* serotype O1, *Listonella (Vibrio) anguillarum* serotype O2a, *Moritella viscosa* and IPNV, and are established active substances. The active substances are manufactured in accordance with the principles of good manufacturing practice.

Starting materials of non-biological origin used in production comply with Ph. Eur.

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. 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.

The packaging also complies with the relevant guidelines.

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 the results of 3 consecutive runs, conforming to the specifications, are provided.

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 are potency, identification, appearance, emulsion stability, sterility, determination of free formaldehyde and viscosity.

The demonstration of the batch to batch consistency is based on the results of 6 batches produced according to the method described in the dossier. Other supportive data provided confirm the consistency of the production process.

II.F. Stability

The active substances are fully tested to ensure compliance with its specification immediately prior to its use in manufacture of the product.

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.

G. Other Information

Shelf life of the veterinary medicinal product as packaged for sale: 18 months.

Shelf life after first opening the container: use within the same day.

Store and transport refrigerated (2 °C – 8 °C). Do not freeze.

III. SAFETY ASSESSMENT

Data have been provided from safety studies using AquaVac 7 supplemented with studies using AquaVac 6. The products are identical with the exception of Aquavac 7 containing an extra antigen.

Laboratory trials

The safety of the administration of one dose, and an overdose in the target animal is demonstrated in two studies for the administration of one dose and in one study for the administration of a single overdose. The investigation was performed according to the recommendations of Directive 2001/82/EC as amended and the relevant guidelines.

The vaccine is inactivated and thus the specific tests to be performed for live vaccines are not applicable.

Field studies

One study was performed at three different sites to evaluate safety and efficacy. The fish were either administered AquaVac 7 vaccine or a positive control. No abnormal behaviour was observed and there was no difference in growth rate observed. The study concluded that the administration of a single dose is considered safe and support the local reactions as per the SPC.

Ecotoxicity

The applicant provided a Phase 1 environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required. The assessment concluded that the overall risk is negligible. 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

The efficacy of the product has been demonstrated in laboratory studies in accordance with the relevant requirements.

Efficacy was based on Relative Percentage Survival according to the specific Ph. Eur, monographs.

Eleven studies were provided in support: two studies for onset of immunity and nine studies which evaluated the bacterial components, four of which determined the onset of immunity, four the serological response to vaccination and one the duration of immunity.

Onset of Immunity

Viral Component

Two studies were provided to assess the onset of immunity, where different batches of the vaccine were investigated to evaluate efficacy and dose response. The relative percentage survival was calculated to confirm efficacy and resolved an onset of immunity of 608 degree days.

Bacterial Component

Four studies were carried out to investigate the onset of immunity of the bacterial components of the vaccine where fish were either administered the vaccine or a saline control. The relative percentage survival was calculated to confirm efficacy and resolved an onset of immunity of 500 degree days.

Dose response studies

Bacterial Components

Four studies were provided to evaluate the dose response of the different bacterial components following vaccination. It was demonstrated that batches containing $\geq 4\%$ of the antigen induced a statistically significant level of protection compared to the control group.

Duration of Immunity

Duration of immunity was demonstrated in laboratory studies up to 16 months and in field studies up to 18 months.

Field Trials

One field study was performed to evaluate safety and efficacy and it was shown that there was protection 18 months post vaccination.

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 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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