IPAR

Publicly Available Assessment Report for a Veterinary Medicinal Product

AQUAVAC PD emulsion for injection for Atlantic salmon

PRODUCT SUMMARY

EU Procedure number	IE/V/0367/001/DC
Name, strength and pharmaceutical form	AQUAVAC PD emulsion for injection for Atlantic salmon
Active substance(s)	Salmon pancreas disease virus (strain F93-125) inactivated
Applicant	Intervet International B.V. Wim de Körverstraat 35 5831 AN Boxmeer The Netherlands
Legal basis of application	Application in accordance with Article 12(3) of Directive 2001/82/EC, as amended.
Date of Authorisation/ completion of procedure	29th March 2017
Target species	Atlantic salmon (*Salmo salar* L)
Indication for use	For active immunisation of Atlantic salmon to reduce viraemia, heart lesions and mortality due to infection with SPDV (pancreas disease). Onset of immunity: 500 degree days. Duration of immunity: Reduction of viraemia: 10 months Reduction of heart lesions: 12 months Reduction of mortality: not established.
ATCvet code	QI10AA01
Concerned Member States	NO, UK

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the HPRA at the end of the evaluation process and provides a summary of the grounds for approval of the marketing authorisation for the specific veterinary medicinal product. It is made available by the HPRA for information to the public, after the deletion of commercially confidential information. The legal basis for its creation and availability is contained in Article 25.4 of EC Directive 2001/82/EC as amended by Directive 2004/28/EC for veterinary medicinal products. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the product for marketing in Ireland.

The Summary of Product Characteristics (SPC) for this product is available on the HPRA's website.

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

II. QUALITY ASPECTS

A.Qualitative and Quantitative Particulars

The product contains inactivated salmon pancreas disease virus (strain F93-125) inducing = 80% RPP (relative percent protection) in a laboratory test in Atlantic salmon. The excipients are light liquid paraffin, polysorbate 80, sorbitan monooleate

and phosphate buffered saline.
The container/closure system consists of bottles of polyethylene terephthalate (PET) closed with a rubber stopper and aluminium cap.

The choice of the adjuvant, vaccine strain, formulation, inactivating agent and 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 at a licensed manufacturing site.

Process validation data for the manufacturing process has been presented in accordance with the relevant European guidelines.

C.Control of Starting Materials

The active substance, inactivated salmon pancreas disease virus (strain F93-125) 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 has been provided.

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

Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies

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.

D.Control Tests during Production

The tests performed during production are described and the results of 3 consecutive runs, conforming to the specifications, are provided.

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 physical tests (appearance, viscosity, visual inspection for type of emulsion and accelerated stability) as well as tests for identity and potency, free formaldehyde and sterility.

The demonstration of the batch to batch consistency is based on the results of 4 batches produced according to the method described in the dossier. Other supportive data provided confirm the consistency of the production process.

F.Stability

Stability data on the active substance has 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 has 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

Not applicable.

III. SAFETY ASSESSMENT (for immunologicals only)

All batches used in the safety studies were representative of the production process. The dose to be used was that recommended for use and contained the maximum antigen content to be included in the finished product. Studies were performed in accordance with the requirements of Directive 2001/82/EC, as amended, and the relevant guidelines.

Laboratory Trials

The safety of the administration of one dose in the target species was demonstrated in several studies. A claim for concurrent use with another vaccine is proposed; use of Aquavac PD at least 240 degree days or 3 weeks before the administration of the MAH's multivalent vaccine Norvax Minova 6, in countries where this vaccine is authorised. As a consequence, the safety studies were conducted with groups of fish vaccinated with a single dose alone, or concurrently with Norvax Minova 6.

For the assessment of safety, the following parameters have been studied:
-Acute toxicity (mortality, behaviour)
-Local reactions (adhesions, melanisation) and vaccine remnants
-Growth performance

The safety of one dose was investigated in Atlantic salmon with average weights close to or at the minimum recommended weight in four studies which differed in the temperature at which fish were held post-vaccination (12°C or 17°C) and the length of the monitoring period post-vaccination (from 3 weeks to 13 weeks). In these studies, fish received one dose of vaccine alone, one dose of vaccine simultaneously with one dose of Norvax Minova 6 (which represented a worst case scenario for safety evaluation, but is not in accordance with recommended use), or one dose concurrently with Norvax Minova 6. The fish were observed daily for mortality or abnormal behaviour. All fish were euthanised at the end of the respective monitoring period and local reactions recorded at autopsy were graded according to the Speilberg scoring system.

The investigations were performed according to the recommendations of Directive 2001/82/EC, as amended, and the relevant guidelines.
No vaccine-related mortality, systemic reactions or abnormal behaviour were observed in the safety studies. In the abdominal cavity, vaccine residues and mild melanisation that is possible to remove were very commonly observed in studies. Visceral adhesions were observed; Speilberg scores of 1 and 2 were very commonly observed and score 3 was commonly observed in studies.
The adhesions observed in the laboratory studies are considered acceptable for fish vaccines.

Based on the results of the studies, it was concluded that the frequency and severity of adverse reactions are increased slightly when Aquavac PD is given in association with Norvax Minova 6. After concurrent use with Norvax Minova 6, in the abdominal cavity, vaccine residues and mild melanisation that is possible to remove were very commonly observed in studies. Unremovable melanisation was commonly observed in studies. Visceral adhesions were observed; Speilberg scores of 1 to 3 were very

commonly observed and score 4 was uncommonly observed in studies.
Appropriate warnings have been placed in section 4.6 (Adverse reactions) and 4.8 (Interactions) of the SPC.
The safety of the administration of an overdose was not investigated because Aquavac PD is an inactivated vaccine and therefore no overdose testing is required.

The safety of the repeated administration of one dose in the target animal was not investigated because the vaccine is recommended for single use only.

No investigation of the effect on reproductive performance was conducted therefore an appropriate warning is included in the SPC (Section 4.7) that the vaccine should not be used in broodstock.

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.

All components included in the product are either of biological origin, are approved food additives or are listed in Annex I (Allowed substances) of Commission Regulation (EU) No. 37/2010 with a 'no MRL required' status. The product does not contain any components in quantities that may be a risk to human health or require an MRL. Based on this information, no withdrawal period is required.

Field Trials

Three studies, conducted at different test sites in Norway, were performed to evaluate the safety and efficacy of Aquavac PD when administered to Atlantic salmon under field conditions. All field studies included a test group vaccinated with Aquavac PD in associated (concurrent or simultaneous) use with Norvax Minova 6 and a positive control group vaccinated with an authorised inactivated pancreas disease vaccine in associated (concurrent) use with Norvax Minova 6. Safety was assessed by evaluating mortality, local reactions and growth performance. The sites selected were stated to be representative of the Norwegian fish industry and had a previous history of pancreas disease.
The fish were monitored from vaccination during the freshwater phase through to sea transfer and harvest, with additional scoring of local reactions at early and late production stages.
The mortality rate in the vaccinated fish was within the normal range expected for commercial fish farms. It was concluded that there were no adverse effects of vaccination on growth performance. The results of the studies, including the

evaluation of local reactions, support those observed in the laboratory studies and indicate that there are no adverse effects of vaccination following concurrent use with Norvax Minova 6 in Atlantic salmon under commercial fish farming conditions over the life span of fish. While no groups of fish vaccinated with Aquavac PD alone were included in the field studies, this is acceptable because it can be considered that the applicant conducted the field studies in conditions that would be expected to be slightly less favourable for the safety evaluation, considering that vaccination was conducted in association with use of another vaccine.
An acceptable safety profile for Aquavac PD under field conditions has been demonstrated.

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 as the product is an inactivated vaccine, there is no risk of spread of live organisms. Neither the active substance nor the excipients are considered hazardous to animals, humans or the environment at the concentrations used. It is accepted that the overall risk to the environment, following use as recommended, is effectively zero.
Warnings and precautions as listed on the product literature are adequate to ensure that the vaccine does not represent a risk to the environment when used as directed.

IV. CLINICAL ASSESSMENT (EFFICACY)

General requirements

The vaccine batches used in the efficacy studies were manufactured in accordance with the production process described in the dossier. Batches with antigen content at the lower limit of the proposed range were used in the laboratory studies.

Laboratory Trials

The efficacy of the product has been demonstrated in several laboratory studies in accordance with the relevant guideline requirements.
Fish of the recommended weight for vaccination were vaccinated according to the recommended schedule for vaccination. Control groups were included in all studies in order to determine the efficacy of vaccination. A Norwegian SPDV isolate was used as the challenge organism in all studies. The route of administration of challenge virus was either by direct intraperitoneal challenge or cohabitation challenge (challenge by cohabitation with infected fish that were shedding virus into water).

Based on data from the laboratory studies, the claims for the reduction in viraemia, heart lesions and mortality caused by pancreas disease are supported. The onset of immunity is 500 degree days. The duration of immunity was demonstrated at 10 months for a reduction in viraemia and 12 months for a reduction in heart lesions.

The duration of immunity for a reduction in mortality due to infection is not established.

Field Trials

Refer to Part III. In the field studies, efficacy was intended to be assessed by evaluation of mortality and growth if an outbreak of pancreas disease occurred. However, for various confounding reasons, including the absence of a negative control group, the field data were not considered sufficiently informative in terms of efficacy evaluation. That said, overall, it was accepted that there were no differences in mortality or growth between the test group and the positive control group during the studies.

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.

VI. 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 Heads of Veterinary Medicines 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.

None.