IPAR

Publicly Available Assessment Report for a Veterinary Medicinal Product

Norvax Compact PD emulsion for injection for Atlantic salmon

"This product was originally authorised under an EU procedure prior to 1st January 2021 where the UK participated as a Concerned Member State. Therefore, the contents of this Public Assessment Report are not owned by the Veterinary Medicines Directorate. Please contact the original Reference Member State for any queries in relation to this report."

PRODUCT SUMMARY

EU Procedure number	IE/V/0257/001/DC
Name, strength and pharmaceutical form	Norvax Compact PD Emulsion for Injection for Atlantic salmon
Active substance(s)	Inactivated salmon pancreas disease virus (SPDV) strain F93-125, 70% RPP* * RPP : relative percentage protection in a laboratory potency test in Atlantic salmon
Applicant	Intervet International BV Wim de Korverstraat 35 5831 AN Boxmeer The Netherlands.
Legal basis of application	Decentralised application in accordance with Article 32(3) of Directive 2001/82/EC as amended.
Date of completion of procedure	22nd June 2011
Target species	Atlantic salmon
Indication for use	For the active immunisation of Atlantic salmon to reduce heart lesions, mortality and weight loss caused by pancreas disease.
ATCvet code	QI10AA01
Concerned Member States	UK, NO

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; any potential adverse effects are detailed in the SPC.

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

II QUALITY ASPECTS

A. Qualitative and Quantitative Particulars

The product is an inactivated, adjuvanted emulsion for injection containing: **Active substance(s):**
Salmon pancreas disease virus (SPDV) strain F93-125, 70% RPP*

* RPP : relative percentage protection in a laboratory potency test in Atlantic salmon

Adjuvant:
Montanide ISA 763A VG

Excipient(s):
Water for Injection
The vaccine is supplied in volumes of 250 ml or 500 ml in polyethylene terephthalate (PET) bottles which are closed with a rubber stopper and a coded aluminium cap.

The choice of the vaccine strain, the adjuvant, the inactivating agent and the absence of a 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 it's 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 on the product have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

Starting materials of non-biological origin used in production comply with the relevant Ph. Eur. monographs. 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 Ph. Eur. monographs and guidelines; any deviation has been 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

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.

D. Control on Intermediate Products

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 tests for potency, sterility and viscosity of the vaccine.
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.

F. 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 broached vaccine is supported by the data provided.

G. Other Information

Not applicable.

III SAFETY ASSESSMENT

The vaccine batches used in the safety studies were manufactured in accordance with the production process outlined in the dossier. The safety of the vaccine has been adequately demonstrated for batches with antigen content ranging from the lower to the upper limits of the antigen content range.

Laboratory Trials

The safety of the administration of one dose and an overdose in the target species is demonstrated in the following studies:

- **Safety of one dose:**

Different groups of Atlantic salmon with average weights close to the minimum recommended weight received one dose of vaccine with antigen contents ranging from the lower to the upper limit of the antigen content range. The fish were observed daily over a 9 week period for mortality or abnormal behaviour.

All fish were euthanized at the end of the 9 week monitoring period and local reactions recorded at autopsy were graded according to the Speilberg scoring system.

- **Safety of an overdose:**

Atlantic salmon of average weight below the minimum weight recommended for vaccination received either a 2x dose of vaccine (of maximum antigen content) or saline. The fish were observed daily over a 21 day period for mortality or abnormal behaviour. All fish were euthanized at the end of the 21 day monitoring period and local reactions recorded at autopsy were graded according to the Speilberg scoring system.

The investigation was 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 single or overdose studies.

Speilberg scores of 1 (very slight adhesions most frequently localised close to the injection site - unlikely to be noticed by laymen during evisceration) were recorded after the single dose administration of Norvax Compact PD, scores of 2 or higher were not observed.

Speilberg scores of 1 - 3 were recorded in the overdose study, with scores of 2 being the most frequently observed after administration of the 2x dose. Administration of an overdose is therefore associated with an increase in the frequency and severity of local reactions compared to a single dose administration.
Appropriate warnings have been placed in section 4.6 (Adverse reactions) of the SPC, and in section 4.10 (Overdose). 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.

The adjuvant used is included in Annex II of Council Regulation No. 2377/90. Based on this information, no withdrawal period is proposed.

The interaction of the vaccine with Norvax Minova 6 was studied. On the basis of the results of this investigation, it is concluded that the frequency and severity of adverse reactions are increased when Norvax Compact PD is given in association with Norvax Minova 6. This is reflected in the SPC (Section 4.8).

Field Studies

One field study, conducted at three different test sites in Norway, was performed to evaluate the safety of Norvax
Compact PD when administered to Atlantic salmon. Both a test group of fish (administered a single dose of Norvax Compact PD on day 0 and a single dose of Norvax Minova 6 on day 21) and a control group (no treatment on day 0; single dose of Norvax Minova 6 on Day 21) were included at each test site.

The fish were monitored from vaccination during the freshwater phase through to sea transfer, at mid production and at harvest.
The mortality rate in the vaccinated fish was within the normal range expected for commercial fish farms (0.05 – 1%) therefore the vaccine is not considered to be associated with an increase in mortality. The frequency and severity of local reactions are increased when Norvax Compact PD is administration in association with Norvax Minova 6 - this is reflected in the SPC (Section 4.8).
An acceptable safety profile for Norvax Compact PD under field conditions has been demonstrated.

Environmental Risk Assessment

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 substances nor the excipients are considered hazardous to animals, humans or the environment at the concentrations used. The assessment concluded that the level of environmental risk is low.

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)

The vaccine batches used in the efficacy studies were manufactured in accordance with the production process described in the dossier. Batches with antigen content ranging from the lower to the upper limits of the proposed range were used in the laboratory studies which is acceptable as the vaccine is classified as a MUMS product and in accordance with the relevant guideline (EMEA/CVMP/IWP/123243/2006-Rev 1: Guideline on data requirements for IVMPs intended for Minor use or minor species/limited markets') there are 'no min/max dose / potency requirements for efficacy studies'.

IV.B Clinical Studies

Laboratory Trials

The efficacy of the product has been demonstrated in 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 such that a total of 485 vaccinated fish and 190 control fish were evaluated in total. A Norwegian SPDV isolate was used as the challenge organism in all studies. Heart lesion scores, mortality and growth rates were measured at appropriate time points after vaccination. The studies supported the efficacy of the vaccine in reducing heart lesions, mortality and weight loss caused by pancreas disease.

Field Trials

One field study, conducted at three different test sites in Norway, was performed to evaluate the efficacy of Norvax
Compact PD when administered to Atlantic salmon. Both a test group of fish (administered a single dose of Norvax Compact PD on day 0 and a single dose of Norvax Minova 6 on day 21) and a control group (no treatment on day 0; single dose of Norvax Minova 6 on Day 21) were included at each test site such that in excess of 300,000 vaccinated fish and 250,000 control fish were included in total.

The fish were monitored from vaccination during the freshwater phase through to sea transfer, at mid production and at harvest for mortality and growth rate.

An outbreak of pancreas disease was confirmed at 2 of the 3 participating sites. The data from these sites are supportive of the reduction in mortality and weight loss claims observed in the laboratory studies. At each of the sites where a disease outbreak occurred, the water temperature ranged from 12 – 13 ºC at the time of vaccination. As there was no outbreak of pancreas disease at the third site where the water temperature was 5 ºC, a statement is included in the SPC advising that the efficacy of the vaccine has not been investigated at low temperatures (e.g. less than 10°C).

Based on data from the laboratory and field studies, the claims for the vaccine in reducing heart lesions, mortality and weight loss caused by pancreas disease and the onset and duration of immunity claims are supported.

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 HPRA website.

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.

Changes: None.