



Paul-Ehrlich-Institut

Beurteilungsbericht zur Veröffentlichung

(gemäß § 31 Abs. 2 Tierimpfstoff-Verordnung)

Poulvac IB Primer

Zulassungsdatum:	06.03.2000
Zulassungsnummer:	167a/88
Datum der Erstellung des öffentlichen Beurteilungsberichts:	15.05.2013
Datum der Bekanntgabe beim Antragsteller der/des Zulassungsänderung/Widerrufs, Rücknahme, Anordnung des Ruhens der Zulassung:	14.05.2013



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MUTUAL RECOGNITION PROCEDURE
PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY
MEDICINAL PRODUCT

Poulvac IB Primer

MODULE 1

PRODUCT SUMMARY

EU Procedure number	DE/V/0259/001/MR
Name, strength and pharmaceutical form	Poulvac IB Primer Lyophilisate for administration as spray, eye-drops or in drinking water, following reconstitution in water
Applicant	Pfizer Ltd. Ramsgate Road, Sandwich, Kent CT13 9NJ, UK
Active substance(s)	Avian Infectious Bronchitis
ATC Vetcode	QI01AD07
Target species	chicken
Indication for use	For active immunisation against Infectious Bronchitis.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Veterinary Medicines Agencies website (<http://www.HMA.eu>).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	MRP application in accordance with Article 32 (2) of Directive 2001/82/EC as amended.
Date of completion of the original mutual recognition procedure	24.04.2013
Date product first authorised in the Reference Member State (MRP only)	06.03.2000
Concerned Member States for original procedure	BG, RO, SI

I. SCIENTIFIC OVERVIEW

The product is produced and controlled using validated methods and tests, which ensure the consistency of the product released onto 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 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 risk/benefit analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Composition

The product contains as active substance:

Live, attenuated Avian Infectious Bronchitis Virus Strain H120:

3.0 – 5.4 log₁₀ EID₅₀

Live, attenuated Avian Infectious Bronchitis Virus Strain D274 Clone:

3.0 – 5.4 log₁₀ EID₅₀

As excipients:

D-Mannitol

Gelatin

Myo-inositol

NZ case plus

The container/closure system consists of Type I glass vials closed with a butyl rubber stopper and aluminium cap. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the vaccine strains is justified.

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.

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

C. Control of Starting Materials

The active substance is a live avian infectious bronchitis virus an established substance described in the European Veterinary Pharmacopoeia. The active substance 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 have been provided.

Biological starting materials used in the vaccine are in compliance with the relevant Ph. Eur. Monographs and guidelines and are appropriately screened for the absence of extraneous agents according to Ph. Eur monograph 2.6.24 and Guideline “Specific requirements for the production and control of avian live and inactivated viral and bacterial vaccines”.

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.

CEP 2000-248 Nutrient Broth

E. Control tests during production

The tests performed during production are described and the results of 3 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; any deviation from these requirements was adequately justified by the Applicant. The tests include in particular

- Visual inspection
- Vacuum testing
- Identification of active substance
- Batch titre
- Safety
- Germ count
- Absence of Mycoplasma spp.
- Absence of extraneous agents in eggs
- Test in CEF
- Absence of CAV using MSB-1 cells
- Test for EDS virus in chicken embryo liver cells
- Test for Marek's Disease Virus in CEF
- Test for Turkey Rhinotracheitis virus in CEF
- Test for Turkey Rhinotracheitis virus in Vero cells
- Residual humidity

The demonstration of the batch to batch consistency is based on the results of 8 batches produced according to the method described in the dossier.

G. Stability

Stability data on the active substance have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions (24 months at -50°C).

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. (18 months at 2-8°C)

The data provided support the in-use shelf-life of the reconstituted vaccine (2 hours).

III. SAFETY ASSESSMENT

Particulars of the vaccine batches used

Laboratory trials

The safety of the administration of one dose and an overdose in the target species is demonstrated in studies where the vaccine was administered with the maximum titre to the most susceptible animals.

The investigation was performed according to the recommendations of Directive 2001/82/EC as amended and the relevant guidelines.

The vaccine was tested in laboratory and field conditions in the target species, i.e. in one day old broilers and layers. The study results indicate that only mild signs of respiratory symptoms (sneezing and coughing) are induced by vaccination. This is reflected in the SPC.

The safety studies of Poulvac IB Primer were assessed on the basis of the current legal requirements for immunological veterinary products. Although some studies are not compliant with the current Ph. Eur. monograph 0442, the provided studies, some conducted for the first marketing authorisation of Poulvac IB primer in 1989, together with data from field studies, present sufficient data to assess the safety of this product. Additionally, PSURs covering the period 2003 to 2011 are provided and no adverse reactions were reported during that period.

The safety of the vaccine strains for chickens of minimum age has been demonstrated.

Effects on reproductive performance were examined in a laboratory and a field study. The laboratory study was not fully compliant with the current legislation, but as no SARs concerning the reproductive performance after vaccination with Poulvac IB Primer were reported during the whole period of marketing, the study is accepted. The field study showed no adverse effects on laying hens revaccinated with Poulvac IB Primer every 6 weeks after onset of lay. The SPC states that: *“The safety of the veterinary medicinal product is not established during lay”*.

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.

For each live strain included in the vaccine the following applies:

Specific studies were carried out to describe the spread, reversion to virulence and biological properties of the vaccine strains. The vaccine strains are able to spread to unvaccinated chickens, therefore the SPC states: *“The vaccine strain may spread to unvaccinated chickens. Safety and reversion to virulence trials have shown that the vaccine strains are safe for chickens. All birds on a site should be vaccinated at the same time.”*

No specific studies were performed to investigate the dissemination of the vaccine strains H120 and D274. This was adequately justified by the Applicant.

There are no known hazards relating to the excipients contained in the finished product. Based on this information, no withdrawal period is proposed.

The interaction of the vaccine with Poulvac NDW was studied. The data was submitted to provide supportive evidence that Poulvac IB Primer is safe in one-day old conventional

chicks. Concurrent use with other vaccines is not claimed by the Applicant. Therefore, the standard sentence is used in the SPC.

Field studies

The first study confirms that a single spray vaccination with Poulvac IB Primer of one-day old broiler chicks under field conditions is safe and only causes mild, transient respiratory sounds in a minority of birds.

The second study was performed in 1985 and is therefore not compliant with the current requirements. Nevertheless, the data provided is sufficient to conclude that vaccination with Poulvac IB primer is safe. No adverse reactions were reported between 2003 and 2011.

The third study confirms that repeated administration of Poulvac IB primer during lay is safe and does not adversely affect the production parameters. The study does not comply with the current requirements, but the beneficial effect of vaccination with Poulvac IB primer can be observed.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that the effect of the product on the environment is minimal and appropriate warnings are included in the SPC and in the product literature. It can be concluded that the use of the immunological veterinary medicinal product Poulvac IB Primer does neither exhibit any environmental risk nor was any precautionary measures deemed necessary.

Warnings and precautions as listed in the product literature are adequate to ensure safety to the environment when the product is used as stipulated.

IV. EFFICACY

IV.B Laboratory Trials

The efficacy of the product has been demonstrated in laboratory studies in accordance with the relevant requirements which show that Poulvac IB Primer is efficacious for protection of day old chickens from challenge with IB Massachusetts and D274 strains.

The experimental challenge models established to compare the efficacy of Poulvac IB Primer in vaccinated and non-vaccinated birds correspond to the provisions stipulated in Ph. Eur. Monograph 0442.

A minimum immunogenicity dose was established for each virus strain and validated in subsequent onset of immunity studies.

The onset of immunity data confirmed the efficacy of Poulvac IB Primer to protect minimum age chicks against both strains contained in the vaccine when administered by eye drop, spray or by drinking water.

Reduction of infection was shown by virus isolation from the trachea and performance of the ciliary activity test.

Furthermore, the onset of immunity studies confirmed that Poulvac IB Primer is efficacious in chickens with MDAs of minimum age, which is the most frequently vaccinated group in the field.

The onset of immunity in two studies was 21 days and in one study 27 days. The Applicant applies for an onset of immunity period of 27 days. This is supported by the provided data.

For component H120 the duration of immunity was demonstrated for 16 weeks. For component D274 a considerable reduction of the impairment of ciliary activity was shown. The reason for the fact that not all control animals showed impairment of ciliary activity after challenge with IB D274 is likely to be an age related resistance to the virus, which is a known phenomenon in the studies with mature animals.

The Applicant applies for a duration of immunity period of 16 weeks. This is supported by the provided data.

Three field studies were conducted the results of which are comparable to the results obtained in the laboratory and confirm that Poulvac IB Primer is efficacious also in large scale use.

The efficacy studies are not entirely compliant with the current legal requirements, although the Applicant has provided additional data and assurance that allow the conclusion that the vaccine is efficacious for its intended use. The data provided are regarded as equivalent to the current legal provisions.

The minimum titre, period of onset of immunity and period of duration of immunity are supported by the data provided.

Field Trials

The applicant has conducted a field study which shows that repeated administration of Poulvac IB Primer during lay was safe and did not adversely affect production parameters. The study does not comply with the current requirements, but the beneficial effect of vaccination with Poulvac IB primer can be observed.

Another field study confirms that a single spray vaccination with Poulvac IB Primer of one-day old broiler and 14-day-old chicks under field conditions is safe and increases the production index on the majority of the farms.

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.