ÚSKVBL
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MUTUAL RECOGNITION PROCEDURE

DRAFT PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Biofel PCH emulsion for injection,

Biofel PCHR emulsion for injection

MODULE 1

PRODUCT SUMMARY

EU Procedure number	CZ/V/0156-0157/001/MR
Name, strength and pharmaceutical form	**Biofel PCH emulsion for injection for cats** **Biofel PCHR emulsion for injection for cats**
Applicant	Bioveta, a. s. Komenského 212/12 683 23 Ivanovice na Hané Czech Republic
Active substance(s)	Inactivated feline panleucopeniavirus Inactivated feline calicivirus Inactivated feline herpesvirus Inactivated rabies virus (only Biofel PCHR)
ATC Vetcode	QI06AA04, QI06AA09
Target species	Cats
Indication for use	Biofel PCH: For active immunisation of cats from the age of 8 weeks against feline panleukopenia, calicivirus and herpesvirus infection. Biofel PCHR: For active immunisation of cats from the age of 3 months against feline panleukopenia, herpesvirus and calicivirus infection and rabies. The onset of protective immunity against panleukopenia is established at 3 weeks after basic vaccination and the onset of protective immunity against feline calicivirus , herpesvirus infection and rabies is established at 4 weeks after basic vaccination. The duration of immunity is 12 months.

Biofel PCH emulsion for injection, Biofel PCHR emulsion for injection	CZ/V/0156-0157/001/MR
Bioveta, a.s.	MRP
	Publicly available assessment report

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	Mutual Recognition application in accordance with Article 32 of Directive 2001/82/EC as amended.
Date of completion of the original mutual recognition procedure	Day 90: 17/04/2019
Date product first authorised in the Reference Member State	01/06/2006 (Biofel PCH) 22/06/2006 (Biofel PCHR)
Concerned Member States for original procedure	SK

I. SCIENTIFIC OVERVIEW

The vaccines Biofel PCH and Biofel PCHR are produced and controlled using validated methods and tests, which ensure the consistency of the products released on the market.

It has been shown that the products can be safely used in the target species.

The products are 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 products was demonstrated according to the claims made in the SPC.

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

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II. QUALITY ASPECTS

A. Qualitative and quantitative particulars

The vaccine Biofel PCH contains inactivated feline panleucopenia virus, inactivated feline calicivirus and inactivated feline herpesvirus.
The vaccine Biofel PCHR contains inactivated feline panleucopenia virus, inactivated feline calicivirus, inactivated feline herpesvirus and inactivated rabies virus.

The adjuvant is Emulsigen (oil adjuvant) and excipient is thiomersal.

The choice of the adjuvant, vaccine strains, substrate for virus multiplication, antigens content in dose, inactivating agent and preservative are justified.
The inactivation process and the detection limit of the control of inactivation are correctly validated.
The products are an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

B. Method of Preparation of the Product

Both products are manufactured fully in accordance with the principles of good manufacturing practice at a licensed manufacturing site.

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

C. Control of Starting Materials

The active substances are inactivated feline panleucopenia virus, inactivated feline calicivirus, inactivated feline herpesvirus and Biofel PCHR additionally contains inactivated Rabies virus.
All the active substances are manufactured in accordance with the principles of good manufacturing practice.

The active substances specification is considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided.
Starting materials of non-biological origin used in production comply with the European Pharmacopeia 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. and European 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.

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 tests during production

The tests performed during production of each antigen and bulk of vaccines are described and the results of 3 consecutive runs (3 batches of each antigen and 3 batches of the bulk of vaccines Biofel PCH and Biofel PCHR), 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:
- appearance
- extractable volume
- sterility
- inactivation test (residual live virus)*****
- identity
- potency
- pH value
- content of thiomersal **
- airtightness
- viscosity

* Performed as in-process control.

** The preservative is added only if the same batch is filled into single- and multi-dose packs.

F. Batch to batch consistency

The demonstration of the batch to batch consistency is based on the results of 6 batches of Biofel PCH and Biofel PCHR (older manufactured in 2010-2011 and newer manufactured in 2015) produced according to the method described in the dossier. Other supportive data provided confirm the consistency of the production process.

G. Stability

Stability data on the active substances have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substances when stored under the approved conditions.

Stability data on the finished products have been provided in accordance with applicable European guidelines, demonstrating the stability of the products throughout its shelf life (2 years) when stored under the approved conditions (2-8°C).

The in-use shelf-life of the broached vaccines (8 hours) is supported by the data provided.

H. Other Information

Non applicable

III. SAFETY ASSESSMENT

Biofel PCH is inactivated vaccine for active immunisation of cats from the age of 8 weeks against feline panleukopenia, calicivirus and herpesvirus infection.

Biofel PCHR is inactivated vaccine for active immunisation of cats from the age of 3 months against feline panleukopenia, herpesvirus and calicivirus infection and rabies.

The vaccines are recommended for cats from the age of 8 weeks or 3 months respectively for 2 injections by subcutaneous administration. The first vaccination with one dose of Biofel PCH in kittens from the age of 8-10 weeks and the second vaccination with one dose of Biofel PCHR from the age of 3 months. The recommended interval between doses is 3 – 4 weeks.
Further regular revaccination with Biofel PCHR is carried out in 12-month intervals.

Vaccination of pregnant cats is recommended in the first half of pregnancy.

Safety studies have been performed with a vaccine batch (Biofel PCH and Biofel PCHR) with maximum antigen content produced according the described production process.

Field studies have been performed with one representative batch of the vaccine Biofel PCH and Biofel PCHR produced according the described production process.

Laboratory trials

The safety of the administration of one dose, one administration of an overdose, the repeated administration of one dose in the target animal (cats) and safety in pregnant cats is demonstrated. The investigation was performed according to the recommendations of Directive 2001/82/EC as amended and the relevant guidelines. No local reactions at the injection site and no clinical changes in the health status were found in cats and pregnant cats.

The following was reported based on post-marketing surveillance experience of Biofel PCH:

Following subcutaneous administration in cats a transient swelling ((usually up to 0.5 cm in diameter), and painfulness) which disappears within 3 weeks may very rarely be observed at the injection site. Transient increase of temperature is very rare after vaccination. In very rare cases hypersensitivity reactions may occur. In such case, appropriate treatment should be initiated without delay.

The following was reported based on post-marketing surveillance experience of Biofel PCHR:

Following subcutaneous administration in cats a transient swelling (usually up to 0.5 cm in diameter) and painfulness which disappears within 3 weeks may very rarely be observed at the injection site. Apathy and anorexia may occur in very rare cases. Transient increase of temperature is very rare after vaccination. In very rare cases hypersensitivity reactions may occur. In such case, appropriate treatment should be initiated without delay.

Effects on reproductive performance were examined. No influence on the process of gestation, birth or progeny was observed during the safety study performed in pregnant animals.

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 and excipients used do not create residues in vaccinated animals. Based on this information, no withdrawal period is proposed.

No specific assessment of the interaction of this product with other medicinal product was made. Therefore, an appropriate warning in the SPC is included.

Field studies

The applicant has performed a study to evaluate the efficacy and safety of the vaccine Biofel PCH and Biofel PCHR under field conditions, in compliance with the principles of Good laboratory Practice (GLP) and Good clinical Practice (GCP).

The safety of the vaccination following the recommended vaccination schedule was evaluated with cats of different sex and age bred by private breeders.
The study included safety assessment after administration of vaccine Biofel PCH and Biofel PCHR according vaccination schedule. The safety evaluation was based on observation of local and systemic reactions.

The safety of the vaccine in cats in the field has been demonstrated. The results from field trials reflect those observed in laboratory trials.

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 there is a negligible risk to the environment associated with use of the vaccine. 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. EFFICACY

All experiments conducted with Biofel PCH and Biofel PCHR in laboratory and field conditions were designed to meet the requirements of the relevant veterinary legislation, including European Directive 2001/82/EC, as amended (2009/9/ES) and relevant European Pharmacopoeia monographs in force.

The efficacy of the products has been demonstrated in laboratory challenge studies on the target species in animals at the minimum age recommended for vaccination (8 weeks for Biofel PCH and 3 months for Biofel PCHR). The vaccine batches with minimum or subminimum antigen content used in the laboratory trials were manufactured using the procedure described in the marketing authorisation documentation.

Field studies have been performed with one representative batch of the vaccine Biofel PCH and Biofel PCHR produced according the described production process.

Laboratory Trials

The efficacy of the products has been demonstrated in laboratory studies in accordance with the relevant requirements which show that the vaccines are intended for active immunisation of cats from the age of 8 weeks or 3 months respectively against feline panleukopenia, herpesvirus, calicivirus infection and rabies.

An overview of laboratory tests:

1) Onset of immunity against feline panleucopenia virus (FPV)
2) Onset of immunity against feline calicivirus (FCV)
3) Onset of immunity against feline herpesvirus (FHV 1)
4) Onset of immunity against rabies virus (RV)
5) Duration of immunity against feline panleucopenia virus 12 months after revaccination
6) Duration of immunity against feline calicivirus 12 months after revaccination
7) Duration of immunity against feline herpesvirus 12 months after revaccination
8) Duration of immunity against rabies virus 12 months after revaccination

Onset of immunity is established at 3 weeks after basic vaccination for feline panleucopenia virus) and at 4 weeks after basic vaccination for calicivirus, herpesvirus and rabies.

Duration of immunity has only been demonstrated after the administration of two vaccine injections (see section 4.9 of the SPC): 12 months after the 2rd vaccine injection (basic vaccination).

Efficacy of vaccination was demonstrated in controlled laboratory challenge studies by challenge each cat intraperitoneally (FPV) or intranasally (FCV, FHV1) or intramuscularly (RV) with a quantity of each virus, sufficient to produce in a susceptible cats characteristic signs of the disease.

The results of the laboratory studies demonstrate full protection for the vaccinated animal against feline panleukopenia, herpesvirus, calicivirus infection and rabies as required by the European Pharmacopoeia monographs 0794, 1207, 1101 and 0451.

Effect of maternal antibodies on the vaccine efficacy has not been studied.

Field Trials

The applicant has performed a study to evaluate the efficacy and safety of the vaccine under field conditions, in compliance with the principles of Good laboratory Practice (GLP) and Good clinical Practice (GCP).

The efficacy of the vaccination following the recommended vaccination schedule was evaluated with cats of different sex and age bred by private breeders.

Efficacy of vaccination in cats was demonstrated including 20 vaccinated cats and 10 unvaccinated controls.

The efficacy evaluation was based on serological profile of antibodies against feline calicivirus, herpesvirus, feline panleucopenia virus and rabies virus.
The field testing demonstrated the satisfactory safety and efficacy of the vaccine Biofel PCH and Biofel PCHR. The results obtained in field studies confirm laboratory trials findings.

V. OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the products are 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 products for humans and the environment is acceptable.

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 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.