



**Institute for State Control of Veterinary Biologicals and Medicines
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(Reference Member State)**

**PUBLICLY AVAILABLE ASSESSMENT REPORT FOR AN
IMMUNOLOGICAL VETERINARY MEDICINAL PRODUCT**

BioEquin FT suspension for injection for horses

Product name: BioEquin FT	Application number: CZ/V/0201/001/MR
Applicant: Bioveta, a.s.	MRP
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PRODUCT SUMMARY

EU procedure number	CZ/V/0201/001/MR
Name and pharmaceutical form	BioEquin FT suspension for injection
Applicant	Bioveta, a.s. Komenského 212/12 68323 Ivanovice na Hané Czechia
Active substance(s)	Influenza A virus, subtype H3N8, strain A/equine/Limerick/2010, inactivated Influenza A virus, subtype H3N8, strain A/equine/Brno/08, inactivated <i>Clostridium tetani</i> , strain Harvard 49205, tetanus toxoid
ATC vetcode	QI05AL01
Target species	Horses
Indication for use	For active immunisation of horses against equine influenza to reduce clinical signs and viral excretion following infection with equine influenza virus and for active immunisation and to prevent mortality against tetanus.

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PRODUCT INFORMATION

The Summary of Product Characteristics (SPC), the labelling and package leaflet for this immunological veterinary medicinal product (IVMP) are available in the Union Product Database (UPD).

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SUMMARY OF ASSESSMENT

Legal basis of original application	Full application in accordance with Article 8 (full dossier) of Regulation (EU) 2019/6.
Date of completion of the original mutual recognition procedure	05/03/2025
Date immunological veterinary medicinal product first authorised in the Reference Member State (MRP only)	04/11/2015
Concerned Member States (CMS) for original procedure	AT, BE, BG, DE, DK, ES, FI, FR, IE, IT, NL, NO, PL, PT, RO, SE, SK, UK(NI)
Withdrawn CMS during original mutual recognition procedure	No.

1. SCIENTIFIC OVERVIEW

The IVMP is manufactured and controlled using validated methods and tests that ensure the consistency of the IVMP released on the market.

The IVMP can be safely used in the target species; the slight reactions observed are indicated in the SPC.

The IVMP is also 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 IVMP was demonstrated according to the claims made in the SPC.

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

2. QUALITY DOCUMENTATION (physicochemical, biological or microbiological information)

2.A. Product description

Each 1 ml dose contains:

Active substances:

Influenza A virus, subtype H3N8, strain A/equine/Limerick/2010, inactivated	min. 5 log ₂ HIT ¹
Influenza A virus, subtype H3N8, strain A/equine/Brno/08, inactivated	min. 5 log ₂ HIT ¹
<i>Clostridium tetani</i> , strain Harvard 49205, tetanus toxoid	min. 30 IU ²

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¹ Serum antibody titre determined in haemagglutination inhibition test after application of one vaccine dose to guinea pigs.

² International units; titre of anti-toxin antibodies, induced after repeated vaccination of guinea pigs according to Ph. Eur., as determined by ELISA.

Adjuvant:

Aluminium hydroxide, hydrated for adsorption 0.2 ml

Excipients:

Thiomersal 0.1 mg
Sodium chloride
Potassium chloride
Potassium dihydrogen phosphate
Disodium hydrogen phosphate dodecahydrate
Water for injections
Sodium hydroxide
Hydrochloric acid

The IVMP is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

The choice of the vaccine strains, adjuvant, inactivating agent, presence of preservative and the formulation is justified.

The selection of the manufacturing process of the active substance and the finished product is explained.

The container/closure system:

The medicine vials are of the hydrolytic class I. Vials of volume 3 ml are closed with rubber stopper and aluminium cap 13 mm. Vials of volume 9 ml are closed with rubber stopper and aluminium cap 20 mm.

Glass vials contain 1 dose or 5 doses of suspension for injection.

Pack sizes:

2 vials of 1 dose
5 vials of 1 dose
10 vials of 1 dose
1 vial of 5 doses
10 vials of 5 doses

The vials with the vaccine are placed in cardboard cartons. In bulk packaging the vials are placed in a PVC package.

2.B. Description of the manufacturing method

The IVMP is manufactured fully in accordance with the principles of good manufacturing practice at a licensed manufacturing site.

Process validation data on the IVMP are provided in accordance with the relevant European guidelines.

2.C. Production and control of starting materials

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The active substances (Influenza A virus strains, *Clostridium tetani*, tetanus toxoid), are the established active substances described in the European Pharmacopeia.

The active substance specifications are considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification are provided.

The master and working seeds were produced according to the seed lot system as described in the relevant guideline.

Biological starting materials used follow the relevant Ph. Eur. monographs and guidelines and are appropriately screened for the absence of extraneous agents according to the Ph. Eur.

Compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products was satisfactorily demonstrated.

Starting materials of non-biological origin used in production comply with indicate pharmacopoeia monographs or in-house specifications.

2.D. Control tests during the manufacturing process

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

2.E. Control tests on the finished product

For all tests, a short description of the techniques for analysing the finished product is provided. The tests and their specifications and limits are justified and are considered appropriate to adequately control the quality of the IVMP.

Satisfactory validation data for each analytical method are provided, if appropriate.

The tests performed on the final product conform to the relevant requirements and monographs, if applicable; any deviation from these requirements is justified. The tests include in particular:

Appearance

Extractable volume

Sterility

Identity and potency**

Inactivation*

Hydrogen ions concentration determination

Content of thiomersal

Air-tightness

Content of Al₂O₃

Residual toxicity**

* Performed as in-process control.

** Performed on bulk of 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.

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2.F. Batch-to-batch consistency

Full protocols of three consecutive batches of the product, representative of the routine production and giving the results for all tests performed during production and on the finished product, are provided in order to ensure that quality is consistent from batch to batch and to demonstrate conformity with the predefined specifications.

2.G. Stability tests

Stability data on the active substance(s) are provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions.

The proposed shelf-life of allantoic fluids with equine influenza antigens is 3 months at - 50 till - 80°C or 21 days at 2-8°C. The proposed shelf-life for both concentrated equine influenza antigens and purified equine influenza antigens is 48 hours at 2-8°C. Inactivated equine influenza antigens can be stored for 11 months at - 50 to - 80°C.

The proposed shelf life of tetanus toxoid is 24 months from the date of manufacture.

Stability data on the finished product are provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions. The 33-months shelf life of the product stored at 2 °C – 8 °C was confirmed.

The in-use shelf life of 10 hours after the first opening of the vaccine is supported by the data provided. The recommendations in the product leaflet should be followed.

The efficacy of the antimicrobial preservation was demonstrated.

2.H. Other information

Not applicable.

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3. SAFETY DOCUMENTATION (safety and residues tests)

3.A. General requirements

The vaccine is administered intramuscularly at dose of 1 ml:

Basic vaccination:

First vaccination from 6 months of age, second vaccination 4 weeks later.

Revaccination:

First revaccination 6 months after basic vaccination and further revaccination is carried out at the latest at intervals of 12 months.

Revaccination of pregnant mares in the last trimester of pregnancy is carried out not later than one month prior to a scheduled foaling date.

The original MA of the vaccine BioEquin FT from 2015 was with the equine influenza strain Morava 95 and the Brno 08 strain. The Morava 95 strain was replaced by the Limerick 2010 strain in 2023 with regard to OIE (WOAH) recommendations. If there was no increase in the number of component strains, specific studies investigating the safety of the modified vaccine are not required according to "Guideline on data requirements for changes to the strain composition of authorised equine influenza vaccines in line with OIE recommendations".

The safety of the vaccine was thus verified on the basis of a laboratory safety studies using the vaccine with the original composition. Safety studies have been performed with a vaccine batch with maximum antigens content produced according to the described production process.

Field studies have been performed with a representative vaccine batch with intermediate antigens content produced according to the described production process.

The safety of the reformulated vaccine was supplemented by monitoring of local reactions and general health observation after vaccination made during efficacy studies with reformulated vaccine BioEquin FT and the safety in field conditions of updated vaccine is monitored within the PSUR.

3.B. Pre-clinical studies

The safety of the administration of double and the repeated administration of one dose to the target animal was demonstrated in the most susceptible category of animals (foals and mares in 3rd trimester of pregnancy).

Safety of administration of double dose and repeated administration of one dose in foal

Study aim	The aim of the study was to assess the safety of the BioEquin FT vaccine with the maximum titre of all antigens after administration by the intramuscular route to animals of four to six month of age.
Animals and application scheme (study groups)	Sixteen healthy unvaccinated foals without antitoxic antibodies and equine influenza virus were enrolled in the study. All animals were intramuscularly administered with a double dose (2 ml) of vaccine with all antigens at the maximum proposed titres. Repeated administrations

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	of a single dose (1 ml) followed every two weeks after first administration, i. e. on Study Days 14 and 28.
Follow-up	Local reactions, general health status and rectal temperature were observed.
Results	No local reactions at the injection site and no clinical changes in the health status were found in foals after administration of the first (a double dose), second and third dose of the test product. Evident rise in rectal temperature values was observed in foals in the time interval of 4 to 24 hours after injection. A gradual decrease in rectal temperature to the level of values before vaccination was recorded between Days 2 and 4 after injection. During the monitoring rectal temperatures did not reach the critical value of 38.8°C, which could be judged as the state of pyrexia.
Conclusion	The safety of vaccine was demonstrated after administration of a vaccine batch with the maximum declared antigen content.

Safety of administration of double dose and repeated administration of one dose in mares in 3rd trimester of pregnancy

Effects on the reproductive performance were also examined in this study.

Study aim	The aim of the study was to assess the safety of the vaccine with the maximum titre of all antigens after administration by the intramuscular route to mare in the third trimester of pregnancy
Animals and application scheme (study groups)	Seventeen healthy mares without antitoxic antibodies and equine influenza virus antibodies were enrolled in the study. All animals were intramuscularly administered with a double dose (2 ml) of the BioEquin FT vaccine with all antigens at the maximum proposed titres. Repeated administrations of a single dose (1 ml) followed two weeks after first administration, i. e. on Study Days 14.
Follow-up	Local reactions, general health status and rectal temperature; for reproductive performance, gestation, parturition and offspring were observed.
Results	No local reactions at the injection site and no clinical changes in the health status were found in mares in the 3 rd trimester of pregnancy after administration of the first and second dose of the test product. A temporary rise in rectal temperatures was recorded after the first and second administration of the tested product to pregnant mares, with maximum values reached 24 hours after injection. During the monitoring, rectal temperatures in pregnant mares did not reach the critical value of 38.8°C, which could be judged as the state of pyrexia. A decrease down to the baseline values was recorded in the next three days. No adverse effects on gestation or on offspring were noted. The course of parturition was uncomplicated in all mares. New-born foals were healthy and viable.
Conclusion	No animal shows abnormal local or systemic reaction or dies from causes attributable to the vaccine. No adverse effects on gestation or of offspring are noted. The course of parturition was uncomplicated and new-born foals were healthy and viable.

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Based on the available PSURs, “site abscess” were added to the table with adverse effects in section 3.6 of the SPC.

The observed reactions are reflected in the relevant SPC and package leaflet sections:

Very common (>1 animal / 10 animals treated):	Injection site swelling. Elevated temperature. ¹
Very rare (<1 animal / 10 000 animals treated, including isolated reports):	Injection site abscess, Anaphylactic reaction. ²

¹ Up to 1 °C for 1-3 days.

² In such a case, symptomatic treatment is required.

Regarding the pregnancy and lactation, the following is stated in the SPC and package leaflet: *“Can be used during pregnancy.*

The safety of the veterinary medicinal product has not been established during lactation.”

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.

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

3.C. Clinical trials

The study included safety assessment after administration of original vaccine according vaccination schedule to foals and pregnant mares.

The clinical study included three farms, in total 22 pregnant mares and 25 foals at the age from 6 months. Besides the animals vaccinated by the tested medicinal product, the clinical study also included the control group of six pregnant mares, not vaccinated during gravidity and the control group of six foals, vaccinated against equine influenza and tetanus by the reference vaccine FLUEQUIN T suspension for injection, for horses.

Application of the tested medicinal product to the pregnant mares was performed in the third trimester of gravidity.

The initial vaccination of foals by the tested medicinal product was performed twice, in the time interval of 28 days. The first revaccination was performed in further six months.

The safety evaluation was based on: observation of local and systemic reactions, measurement of rectal temperatures and evaluation of possible influence of the vaccination on gestation, parturition and progeny.

Neither local reactions at the administration sites nor systemic adverse reactions were observed in both categories of animals after administration of vaccine according vaccination schedule. No increase of body temperature exceeding the physiological limits was recorded. All vaccinated animals remained in a good health condition.

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No negative effect neither on the pregnancy of the mares, nor on the health condition of the progeny was observed during the study.

The safety of the administration of vaccine was demonstrated in field conditions in pregnant mares and foals, confirming results of laboratory studies.

3.D. 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 further assessment was required. The assessment concluded that there is a negligible risk to the environment associated with use of the vaccine.

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

3.E. Assessment required for veterinary medicinal products containing or consisting of genetically modified organisms

Not applicable.

3.F. Residue tests to be included in the pre-clinical studies

The adjuvant and excipients used are aluminium hydroxide and thiomersal. The excipient and adjuvant are included in the Appendix of the Commission Regulation (EU) No 37/2010 – the substances that are not subject to determination of residues. For this reason, the presence of the residues was not tested. Based on this information, no withdrawal period is proposed.

4. EFFICACY DOCUMENTATION

4.A. General requirements

BioEquin FT, suspension for injection for horses, is a veterinary medicinal product intended for active immunization of horses to reduce the virus excretion, clinical signs during the respiratory disease caused by the equine influenza virus subtype A/Equi 2, and active immunisation against tetanus.

Due to the O.I.E. Recommendations for the composition of the equine influenza vaccine an updated BioEquin FT vaccine was developed and prepared in 2022, in which the Eurasian influenza strain (Morava 95) was replaced by the American one (Limerick 2010).

Two strains of equine influenza virus are presented in the updated vaccine BioEquin FT.

American lineage strain:

A/Equi 2/Brno 08 (isolated in the year 2008, A/Equi 2/Richmond/1/2007-like virus)

and

A/Equi 2/Limerick 2010 (isolated in the year 2010, A/Eq/SouthAfrica/04/2003-like virus).

Laboratory trials were aimed on recommended category of target animals mentioned in EP: 0249 – Equine influenza vaccine - foals aged not less than 6-month-old.

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Onset of immunity for strain A/Equi 2/Brno 08 of the vaccine was proved after challenge of the animals in efficacy study with a vaccine with the original composition.

The challenge strain CHSV Bio-25: A/ Equi 2/ Praha 2008 was used. Phylogenetic classification of the virus is identical with that vaccine strain.

Field trials with original vaccine were carried out to confirm the results of efficacy tests using the batch with an intermediate titre of antigens produced according to the described production process.

Onset of immunity for strain A/Equi 2/Limerick 2010 of the vaccine was proved after challenge of the animals in efficacy study with a vaccine with the updated composition.

The challenge virus A/equine/Rio Grande do Sul/1/12 was used. Phylogenetic classification of the virus is identical with that vaccine strain Limerick 2010.

The efficacy in field conditions of updated vaccine is monitored within the PSUR.

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4.B. Pre-Clinical Studies

The efficacy of the product was demonstrated in laboratory studies under well-controlled conditions in accordance with the relevant requirements, which show that the vaccine:

“reduces clinical signs and viral excretion following infection with equine influenza and prevent mortality against tetanus”.

The laboratory efficacy studies included the following evaluation:

Onset and duration of immunity for equine influenza:

- in foals (original vaccine composition) – for strain A/Equi 2/Brno 08;
- in foals (updated vaccine composition) – for strain A/Equi 2/Limerick 2010.

Onset and duration of immunity against tetanus in foals (original vaccine composition).

Onset of immunity against equine influenza in foals – original vaccine composition (A/Equi 2/Brno 08)

Study aim	Onset of immunity
Animals, antibody status, vaccine and application scheme (study groups)	Twelve unvaccinated foals over 6 months of age, without antibodies to equine influenza virus were selected. Seven foals were injected a dose of the vaccine (1 ml) deeply into the neck muscle, twice at an interval of 28 days. Five control foals were not vaccinated.
Vaccine	The batch with minimum antigen content.
Challenge	14 days after the second vaccination, all animals were infected with a virulent challenge strain of equine influenza virus: CHSV Bio-25: A/Equi 2/ Praha 2008 in the form of aerosol.
Follow up / evaluation criteria	Until 14 days post challenge - Rectal temperature - Clinical observation (after vaccine administration and challenge) - Excretion of the challenge virus - Blood samples (serology) The clinical observation focused on changes in the overall health status of foals, respiratory disorders, eye and nasal discharge. Rectal temperatures were measured and nasopharyngeal samples were collected in all foals to determine the amount of excreted virus.
Results	Statistically significant differences were recorded between the vaccinated and the control group of foals in the evaluation of overall clinical symptoms of disease, in the evaluation of rectal temperatures and the duration of virus excretion and the amounts of the virus excreted after challenge. HI titres of antibodies were established on the day of challenge.
Conclusion	The efficacy of the vaccine was demonstrated and 2 weeks onset of immunity after basic vaccination was set.

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Onset of immunity against equine influenza in foals – updated vaccine composition (A/Equi 2/Limerick 2010)

Study aim	Onset of immunity
Animals, antibody status, vaccine and application scheme (study groups)	Twelve unvaccinated foals over 6 months of age, without antibodies to equine influenza virus were selected. Seven foals were injected a dose of the vaccine (1 ml) deeply into the neck muscle, twice at an interval of 28 days. Five control foals were not vaccinated.
Vaccine	The batch with minimum antigen content.
Challenge	14 days after the second vaccination, challenge virus A/equine/Rio Grande do Sul/1/12- Equine influenza virus of Florida sub-lineage 1 was administered to nostrils to both vaccinated and control animals
Follow up / evaluation criteria	<p>Until 14 days post challenge</p> <ul style="list-style-type: none"> - Rectal temperature - Clinical observation (after vaccine administration and challenge) - Excretion of the challenge virus - Blood samples (serology) <p>The clinical observation focused on changes in the overall health status of foals, respiratory disorders, eye and nasal discharge. Rectal temperatures were measured and nasopharyngeal samples were collected in all foals to determine the amount of excreted virus.</p>
Results	<p>The vaccine significantly reduces clinical signs and significantly reduce virus shedding after infection.</p> <p>HI titres of antibodies were established on the day of challenge.</p>
Conclusion	The efficacy of the vaccine was demonstrated and the onset of immunity 14 days after second administration has been verified.

Duration of immunity against equine influenza in foals – original vaccine composition (A/Equi 2/Brno 08)

Study aim	Duration of immunity
Animals, antibody status, vaccine and application scheme (study groups)	<p>Twelve unvaccinated foals over 6 months of age, without antibodies to equine influenza virus, were selected. Seven foals were injected a dose of the vaccine (1 ml) deeply into the neck muscle, twice at an interval of 28 days.</p> <p>6 months later the foals received the third and the fourth dose of the vaccine (booster vaccination) was performed identically 12 months after the third dose. Five control foals were not vaccinated.</p>
Vaccine	The batch with minimum antigen content
Serological monitoring	Until 12 months after fourth dose of the vaccine

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(no challenge)	
Follow up / evaluation criteria	Until 12 months after fourth dose of the vaccine - Clinical observation - Rectal temperature - Blood samples
Results	No local reactions (swelling, fever, pain) were observed after administration of the tested product and no foal of the vaccinated group and the control group manifested signs of disease. Antibody levels determined throughout the study correspond to the established vaccination schedule. The satisfactory antibody titres (determined by SRH and HI test) were achieved in any of the vaccinated animals. Moreover, the post vaccination antibody titre 1:64 has been verified by challenge test in the OOI study with the original vaccine.
Conclusion	The obtained results verify the efficacy of the vaccine, even 12 months after the booster vaccination performed 12 months after the first revaccination.

Duration of immunity against equine influenza in foals – updated vaccine composition (A/Equi 2/Limerick 2010)

Study aim	Duration of immunity
Animals, antibody status, vaccine and application scheme (study groups)	Twelve unvaccinated foals over 6 months of age, without antibodies to equine influenza virus, were selected. Seven animals were vaccinated intramuscularly with 1 ml of the updated vaccine and 5 foals were used as control. Control group was vaccinated with reference item (only tetanus toxoid active substance). On Study Day 0, 28, 208 and 568, the vaccine and reference item were administered in vaccinated and control group. The Study was terminated on day 928.
Vaccine	Vaccine - the batch with minimum antigen content. Reference item - only tetanus toxoid active substance included.
Serological monitoring (no challenge)	Until 12 months after fourth dose
Follow up / evaluation criteria	Until 12 months after fourth dose - Clinical observation - Rectal temperature - Blood samples
Results	No abnormal clinical signs and no local reactions were observed in vaccinated and control animals. One horse died, but from reason not related with vaccination (intestinal colic). Serological examination showed measurable increases of antibodies titre against equine influenza virus A-Equi2-Limerick 2010 in vaccinated animals. The expected increase in antibody titre is noted at further sampling points. The maximum is reached after the fourth administration of the test item. The satisfactory antibody titres were achieved in any of the vaccinated animals. The OIE requirement was met throughout the

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	study after the 2nd application of the test item, where no sample had a HI titer of less than 64.
Conclusion	The obtained results verify the efficacy of the vaccine, even 12 months after the booster vaccination performed 12 months after the first revaccination.

Effect of reformulated vaccine on immunogenicity of other components

Based on an additional comparison of serological results for the Brno 08 EIV strain and tetanus anatoxin it was verified that the new equine influenza virus antigen Limerick 2010 in the updated vaccine has no potentiating effect on the immunogenicity of the equine influenza virus antigen Brno 08 and tetanus toxoid in the updated vaccines BioEquin FT.

Onset and duration of immunity against tetanus– original vaccine composition (Brno+Morava)

Study aim	Onset and duration of immunity
Animals, antibody status, vaccine and application scheme (study groups)	<p>Twelve unvaccinated foals over 6 months of age without antibodies against tetanus at the age of at least 6 months have been chosen for testing.</p> <p>Seven foals were injected a dose of the vaccine (1 ml) with the minimum antigen content deep into the neck muscle, twice at an interval of 28 days. Another 6 months later the foals received the third and the fourth dose of the vaccine - booster vaccination was performed identically 12 months after the third dose. Five control foals were not vaccinated.</p> <p>On Study Day 0, 28, 209 and 575, the vaccine as outlined in Study Design (Table 5) was administered in vaccinated group by the examining veterinary surgeon. The vaccine was always administered deep intramuscularly into the left neck muscle in a dose of 1.0 ml by means of standard aseptic technique.</p>
Vaccine	Two vaccine batches with minimum antigen content
Serological monitoring (no challenge)	Until 12 months after fourth dose
Follow up / evaluation criteria	<p>Until 12 months after fourth dose</p> <ul style="list-style-type: none"> - Clinical observation - Rectal temperature - Blood samples <ul style="list-style-type: none"> • Dynamics of antibodies against tetanus in the serum samples was determined by the ELISA method. • Protective level of antibodies (at least 0.1 IU), in the serum samples was determined by the challenge test (TNT – toxin – neutralization test) on mice.

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Results	<p>No local reactions (swelling, temperature, pain) and no other symptoms of the disease were observed in any animal of neither the vaccinated or control group.</p> <p>Initial serum samples of the control and vaccinated foals' titres of antibodies against the tetanus toxin were determined with negative results.</p> <p>Further examination was performed in the samples taken during the study period.</p> <p>In all foals of the control non-vaccinated group results of antibodies examination were negative. In the vaccinated foals on the 14th day after the basic vaccination values of antibodies reached >15 IU / ml.</p> <p>One year after the first revaccination, i.e. at the moment of application of the booster and 12 months after the booster values of antibodies against the tetanus toxin were in all samples of the vaccinated animals >0.5 IU/ ml.</p> <p>Assessment of efficiency was proved on the basis of the determined level of antibodies (IU in ml of sera), and the values from 0.1 to 0.5 IU per ml were considered protective. This assessment was determined on the basis of the literature data and is based on passive protection of horses after the challenge by the tetanus toxin (Patočka et al 1974). Much lower protective level > 0.02 IU/ml is shown by Heldens et al, 2001, in his vaccination study.</p>
Conclusion	<p>The obtained results document onset of immunity against tetanus 14 days after the basic vaccination, and duration of immunity for 6 months after the basic vaccination and 12 months after application of the booster.</p>

Influence of maternally derived antibodies

Interference of maternal antibodies at vaccination of foals against equine influenza and tetanus has been demonstrated and is described in the professional literature. Based on this, the vaccination of the foals born to regularly vaccinated (or more than twice) mothers is recommended from the age of at least six months (24 weeks).

4.C. Clinical trials

Efficacy of vaccination was also demonstrated under field conditions in a controlled field trials.

The clinical study was started in three farms, in total in 22 pregnant mares and in 25 foals at the age from 6 months of age. Besides the animals vaccinated by the tested medicinal product, the clinical study also included the control group of six pregnant mares, not vaccinated during gravidity and the control group of six foals, vaccinated against equine influenza and tetanus by the reference vaccine FLUEQUIN T suspension for injection, for horses.

Application of the tested medicinal product to the pregnant mares was performed in the third trimester of gravidity.

The initial vaccination of foals by the tested medicinal product was performed twice, in the time interval of 28 days. The first revaccination was performed in further six months.

Monitoring of efficacy in the field conditions was focused on possible symptoms of respiratory diseases corresponding to the equine influenza virus and CNS disorders corresponding to the

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tetanus disease, but mainly on examination of specific antibodies in blood samples. The level of antibodies against antigens of the equine influenza virus represented in the vaccine was determined by the method of SRH and by the haemagglutination inhibition test in foals. Dynamics of antibodies against tetanus was determined by the ELISA method.

Results of serological examination of the pregnant mares and newborn foals

Equine influenza

No significant difference between the values of antibodies against the equine influenza virus A/Equi 2/Brno 08 were established between the vaccinated and the control mares at time of vaccination. On the other side, differences between values of in the vaccinated group and in the control group of the pregnant mares were statistically significant after vaccination during the birth.

The pair correlation between values of antibodies against the equine influenza virus A/Equi 2/Brno 08 was proved during the birth in the vaccinated mares and in the foals. Based on the established data, it has been proved that the vaccinated mares were protected actively against infection by the equine influenza virus during the pregnancy and during the next period of lactation the mother antibodies were handed over to the foals.

The level of maternal antibodies was also monitored in the newborn foals, namely from the birth till the sixth month of age - in monthly intervals. Protective level of antibodies against the equine influenza virus A/Equi 2/Brno 08 was proved in 21 foals after the birth and colostrums drinking.

Tetanus

In the pregnant mares' values of antibodies ranged at the moment of application of the vaccine from 2.0 to 9.8 IU (average value – 4.48 IU). During the birth the average value of antibodies was 23.745 IU (range from 19.1 to 27.8 IU). Only in one of the mares a low value of antibodies (3.8 IU) was established.

In twenty newborn foals the level of antibodies ranged after the birth from 14.2 to 31.1 IU. During the next month decrease of antibody values were recorded in these foals, till the sixth month of monitoring. In one foal after the birth a low value of antibodies was recorded.

In the control non – vaccinated group of mares, in the ninth month of gravidity, the average value of antibodies against tetanus 4.7 IU (range 2.5-7.7 IU) was determined. Shortly after the birth, the average value of antibodies 3.9 IU (range 2.3-6.1) was determined in the mares and 2.65 IU (range 0-4.2) in the foals.

By statistical analysis during the 9th month of gravidity no significant difference between the values of the control and the vaccinated group of mares was proved. On the other side, during the birth the difference in values of antibodies against tetanus in the vaccinated and the control group was statistically significant. Correlation was recorded also between values of antibodies in the mares and in the newborn foals (after the birth).

Results of serological examination in the foals

Equine influenza

By statistical assessment of growth of antibodies after the basic vaccination, difference between the foals vaccinated by the tested medicinal product BioEquin FT and the foals vaccinated by the reference vaccine FLUEQUIN T was proved. A significant different in growth of antibodies was also reported between the two groups vaccinated by the medicinal product BioEquin FT, though at the boundary of assessment. By assessment of growth of antibodies against equine influenza antigen A/Equi 2/Brno 08, no statistically significant differences were recorded between individual groups of foals after application of the 3rd dose of vaccine.

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Publicly available assessment report	

Tetanus

Low levels of mother antibodies against tetanus were proved before the first injection (range 0.3-3.1 IU). Significant rise of antibodies was reported in all foals within 14 days after the second vaccination. Within six months after the second vaccination, before the 3rd application of the vaccine, the level of antibodies dropped markedly, compared with the initial level (average value of 3.187 IU). After application of the 3rd injection explicit growth of antibodies was recorded – up to the average value 17.974 IU. Then the dynamics of antibodies was of descending character. One year after application of the 3rd dose of vaccine the average value of antibodies was as low as 2.795 IU.

In the foals of the control group, vaccinated by the reference vaccine FLUEQUIN T, low values of antibodies against tetanus were established during the first application of the vaccine (average 1.1 IU). The dynamics of antibodies against tetanus is similar to the course reported in the foals vaccinated by the BioEquin FT. Significant growth of antibodies was recorded within the 14th day after the second vaccination. The average level of antibodies was 22.8 IU (the values ranged from 17.3 to 25.7 IU) and during the next period decrease of the antibodies level was monitored. At the moment of application of the 3rd injection the average value amounted to 5.05 IU. Two months after growth of antibodies up to the average value of 12.2 IU (range 9.1- 14.5 IU) was recorded. Then the dynamics of antibodies was of descending character and 12 months after the 3rd vaccination the average value of antibodies was 1.8 IU (range 1.3 – 2.5 IU).

By statistical assessment of growth of antibodies after the basic vaccination no significant difference was proved between the groups of foals that were vaccinated by the tested medicinal product BioEquin FT and the group of foals vaccinated by the reference vaccine FLUEQUIN T. Even, after application of the booster (1st revaccination) significant difference in growth of antibodies was not proved between individual groups.

For booster application of vaccine (4th vaccination) were selected 19 foals. Interval between 3rd application of vaccine BioEquin FT and booster was 12 months. Six months after booster vaccination, the mean value of antibodies to equine influenza virus A/Equi 2/Brno 08 was 128,6 mm² (range 113 – 141). Twelve months after booster vaccination, the determined value of antibodies to equine influenza virus A/Equi 2/Brno 08 105.78 (rang 96.7-114.9). By haemagglutination inhibition test examination, 6 months after booster, the titre of antibodies to equine influenza virus Brno 08 ranged from 7 to 9 log₂, the mean value for A/Equi 2/Brno 08 was 7.84 log₂. One year after booster, the titre of antibodies to equine influenza virus Brno 08 ranged from 6 to 8 log₂, the mean value A/Equi 2/Brno 08 was 6.74 log₂. The values of antibodies to tetanus, ranged 6 months after application of the booster from 4.2 to 6,5 IU and the mean value was 5.39 IU. One year after application of the booster, the values ranged from 2.7 to 4.9 IU and the mean value was 3.8 IU).

The efficacy in field conditions of updated vaccine is monitored within the PSUR.

Product name: BioEquin FT	Application number: CZ/V/0201/001/MR
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5. 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 are acceptable.

Product name: BioEquin FT	Application number: CZ/V/0201/001/MR
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POST-AUTHORISATION PROCEDURES

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/labelling/package leaflet is/are available in the Union Product Database (UPD).