ÚSTAV ŠTÁTNEJ KONTROLY VETERINÁRNYCH BIOPREPARÁTOV A LIEČIV
Institute for State Control of Veterinary Biologicals and Medicaments
Biovetská 34, 949 01 Nitra, Slovak Republic

Tel.: +421/37/ 651 506-7
Fax.:+421/37/ 651 7915
IČO: 31 873 154

www.uskvbl.sk
email: uskvbl@uskvbl.sk
DIČ: 20212703

Administrative Code: 2340/18-Sk *Certificate Number: R-175/18/OB/OCABR* *Date: Nitra,* 11. 10. 2018

EUROPEAN COMMUNITY/EEA OFFICIAL CONTROL AUTHORITY BATCH RELEASE CERTIFICATE FOR IMMUNOLOGICAL VETERINARY MEDICINAL PRODUCTS

CERTIFIKÁT EURÓPSKEHO SPOLOČENSTVA/EEA O ÚRADNOM UVOĽNENÍ ŠARŽE IMUNOLOGICKÉHO VETERINÁRNEHO LIEKU

Examined under the Article 82 of Directive 2001/82/EC as amended by Directive 2004/28/EC and in accordance with the current Procedure for Official Control Authority Batch Release of immunological veterinary medicinal products in the European Community. *(Kontrolovaný podľa článku 82 Smernice 2001/82/ES v znení Smernice 2004/28/ES a v súlade s aktuálnym pokynom Postup pre úradné uvoľňovanie šarží imunologických veterinárnych liekov v Európskom spoločenstve)*

Trade name *(obchodný názov)*	**Columba emulsion for injection** (Columba PPMV-1; Columba vakcina A.U.V.)
International non-proprietary Name /Ph.Eur. name/common name *(medzinárodný nechránený názov/Ph.Eur. názov /bežný názov)*	Vaccinum pseudopestis aviariae inactivatum
Name and address of marketing authorisation holder *(meno a adresa držiteľa rozhodnutia o registrácii)*	Pharmagal Bio, s.r.o. Murgašova 5, 949 01 Nitra, Slovak Republic
Name and address of manufacturer, responsible for batch release *(meno a adresa výrobcu zodpovedného za uvoľnenie šarže)*	Pharmagal Bio, s.r.o. Murgašova 5, 949 01 Nitra, Slovak Republic
Marketing authorisation number (Member State/EC) *(číslo rozhodnutia o registrácii -členský štát/ES)*	BE - V 330552 (BE) REG NL 102076 (NL) 97/042/07-C (CZ) 1775/07 (PL) PEI.V.03546.01.1 (DE) 97/016/07-S (SK) 2232/2/07 MgSzH ÁTI (50 adag) (HU)
Manufacturer's batch number appearing on package and other identification numbers associated with this batch *(číslo výrobnej šarže a ďalšie súvisiace identifikačné čísla)*	86 03 18 02 (Final batch from the Bulk 86 03 18)
Batch number of diluent (where appropriate) *(číslo. šarže riedidla)*	-
Type of container *(druh obalu)*	Glass vials (type I) closed with chlorobutyl rubber stopper and sealed with aluminium cap.
Total number of containers in this batch *(veľkosť šarže)*	5516 pcs.
Number of doses/volume per container *(počet dávok/objem)*	50 vaccine doses / 15 ml
Date of start of period of validity *(dátum začiatku doby platnosti)*	07.03.2018

This batch has been examined in conformity with the above-mentioned procedure. This examination is based on review of the manufacturer's protocol and repetition of the appropriate control laboratory tests. The testing has been carried out under a quality system which is in accordance with ISO/IEC 17025.
(Táto šarža bola skúšaná podľa vyššie uvedených postupov. Výsledky sú založené na kontrole protokolu výrobcu a opakovaní príslušných kontrolných laboratórnych testov. Skúšanie bolo vykonávané v systéme kvality, v súlade s normou ISO/IEC 17025)

This batch **–IS– in compliance** with the approved specifications laid down in the above-mentioned marketing authorisation. Technical details of these compliance results are annexed to this form. *(**Táto šarža –JE – v súlade** s údajmi uvedenými v registračnom rozhodnutí tohto imunologického veterinárneho lieku. Technické údaje získaných laboratórnych výsledkov sú v prílohe tohto rozhodnutia)*

Signed *(podpísal)*:

Name and function of signatory:
(meno a funkcia podpisujúceho)

ÚSTAV ŠTÁTNEJ KONTROLY veterinárnych biopreparátov a liečiv NITRA

MVDr. Judita Hederová, PhD.
Director of Institute

ANNEX - TEST REPORT

Príloha – Správa o skúšaní

Trade name *(obchodný názov)*	**Columba emulsion for injection** (Columba PPMV-1; Columba vakcina A.U.V.)
Name and address of marketing authorisation holder *(meno a adresa držiteľa rozhodnutia o registrácii):*	Pharmagal Bio, s. r. o., Murgašova 5, 949 01 Nitra, Slovak republic
Marketing authorisation number (Member State/EC) *(číslo rozhodnutia o registrácii -členský štát/ES)*	BE - V 330552 (BE) 97/042/07-C (CZ) PEI.V.03546.01.1 (DE) 2232/2/07 MgSzH ÁTI (50 adag) (HU) REG NL 102076 (NL) 1775/07 (PL) 97/016/07-S (SK)
Manufacturer's batch number appearing on package *(číslo výrobnej šarže uvedenej na obale)*	**86 03 18 02**
Expiry date *(dátum exspirácie)*	6.9.2019

Results *(výsledky)*:

Method (SOP) *(postup ŠPP)*	**Appearance** (OB-UŠ-01.1)
Date of testing *(dátum skúšania)*	04.10.2018
Limit/Specifications *(popis)*	White to light yellow emulsion with easily shakeable sediment.
Result *(výsledok)*	conform to specifications
Method (SOP) *(postup ŠPP)*	**Potency test** (OB-UŠ-01.2)
Date of testing *(dátum skúšania)*	03.04. – 26.04.2018
Limit/Specifications *(požadované hodnoty)*	average titer fixed: 1 full dose : 5,81 – 12,31 $\log_2$ HI units 1:5 dose : 4,88 – 10,84 $\log_2$ HI units 1:10 dose : 2,77 – 8,87 $\log_2$ HI units
Results *(výsledky)*	1 full dose : pass 1:5 dose : pass 1:10 dose : pass

Note *(poznámka)*:

The test results for potency have been obtained on final bulk 86 03 18 *(Výsledky skúšky účinnosti boli stanovené vyšetrením hotového bulku č. 86 03 18)*

Nitra, 10. 10. 2018

MVDr. Katarína Massányiová, PhD.
Head of Department of Biologicals
(vedúci odboru biopreparátov)

PHARMAGAL BIO s.r.o., Nitra, SR
Producer of immunological veterinary medicinal products
Murgašova 5,
949 01 Nitra, SR
tel. / fax : +421 37 65 33 171
bio@pharmagalbio.sk

ANALYTICAL CERTIFICATE

COLUMBA PPMV1
COLUMBA vakcina A.U.V.
COLUMBA

Batch: 86 03 18 02

Expiry: 06.09.2019

TESTS	METHODS	STANDARD	RESULT
Biological parameters			
Sterility	534-III/07	Absence of growth of micro-organisms	Absence of growth of micro-organisms
Potency In chickens, post-vaccination serology to gradually diluted vaccine dose	534-III/09	Mean HI titres must comply with the standards related to the dose applied: 5.81 – 12.31 $\log_2$ HI (full dose) 4.88 – 10.84 $\log_2$ HI (1:5) 2.77 – 8.87 $\log_2$ HI (1:10)	Full vaccine dose: 9.00 $\log_2$ HI Equivalent to 1:5: 6.40 $\log_2$ HI Equivalent to 1:10: 5.20 $\log_2$ HI
Identity In chickens / Serology	534-III/10	Formation of antibodies specific to the vaccine virus.	Formation of antibodies specific to the vaccine virus.
Extraneous viruses In chickens / Serology	534-III/11	Absence of extraneous viruses.	Absence of extraneous viruses.
Inactivation In vitro in embryonated SPF eggs.	534-III/12	Absence of replication of the vaccine virus.	Absence of replication of the vaccine virus.
Physicochemical parameters			
Appearance	534-III/05	Emulsion of white to light-yellow colour. Formation of easily shakeable sediment is allowed.	Emulsion of white to light-yellow colour. Formation of easily shakeable sediment is allowed.
Extractable volume	534-III/06	15 ml	15 ml
pH value	534-III/13	pH 6.50 – 7.50	pH 6.86
Content of thiomersal	534-III/14	0.08 – 0.12 g/l	0.11 g/l
Stability of emulsion	534-III/15	Emulsion is stable.	Emulsion is stable.
Viscosity	534-III/16	25.7 – 28.5 mPa.s	28.42 mPa.s

- CONFORMING -

This is to declare that **COLUMBA, Batch 86 03 18 02** was manufactured and tested and complies with the quality requirements given in Marketing Authorization Dossier of COLUMBA as they were approved by the competent authorities and that all measures have been taken to demonstrate compliance with Directive 2001/82/EC as amended by Directive 2009/9/EC.

Nitra, August 23, 2018

PHARMAGAL BIO s.r.o.
Murgašova 5
949 01 NITRA

MVDr. Denisa Svitačová
Quality Control Laboratory

ŽIADOSŤ O ÚRADNÉ UVOĽNENIE ŠARŽE IVL NA TRH EÚ

Request for OCABR – Procedure for a harmonised application of art. 82 for official batch release of IVMP in the EU

According to Art. 82 of Council Directive 2001/82/EC amended by Directive 2004/28/EC

Protokol výrobcu o šarži lieku

MANUFACTURERS BATCH PROTOCOL

1. Všeobecné informácie

MEMBER STATE SPECIFIC INFORMATION

Žiadateľ Meno a adresa žiadateľa/držiteľa registračného rozhodnutia *Name and address of marketing authorisation holder*	Pharmagal Bio, s. r. o., Murgašova 5 949 01 Nitra
Výrobca (meno, adresa výrobcu) ak sa líši od držiteľa *Name and address of manufacture, if different*	Pharmagal Bio, s. r. o., Murgašova 5 949 01 Nitra
Obchodný názov imunologického veterinárneho lieku *Trade name:*	COLUMBA, COLUMBA PPMV1 COLUMBA vakcina A.U.V.
Medzinárodný názov / liekopisný / všeobecný názov *International non-proprietary Name / Ph. Eur. name / common name*	Vaccinum pseudopestis aviariae inactivatum ATCvet. code: QI 01EA01
Lieková forma *Pharmaceutical form of finish. prod.*	Emulsion for injection
Skladovacia teplota *Storage temperature*	+2 - +8°C Do not freeze.
Registračné číslo a dátum vydania registračného rozhodnutia pre vakcínu/riedidlo *Marketing authorisation number for vaccine/diluent (Member State / EC) issued by*	Belgium BE-V 330522 Czech Republic 97/042/07-C Germany PEI.V.03546.01.1 Hungary 2232/2/07 MgSzH ÁTI (50 agad) Nethelands REG NL 102076 Poland 1775/07 Slovak republic 97/016/07 – S

2. Súhrnné informácie o šarži hotového výrobku

SUMMARY INFORMATION ON THE FINAL BATCH OF FINISHED PRODUCT

Číslo šarže vakcíny *Manufacturer's batch number(s) appearing on package and other identification numbers associated with this batch (final bulk no, final lot no, packaging lot no)*	**86 03 18 02** Final batch from Bulk - **86 03 18**
Číslo šarže riedidla *Batch nr. of diluent (where appropr.e)*	Not appropriate
Druh obalu *Type of container:*	Glass vials (hydrolytic resistance Type I), rubber chlorobutyl stoppers and aluminium cap with central tear-off
Veľkosť šarže a počet obalov pre jednotlivé veľkosti balenia *Total number of containers in this batch*	5 516 pcs
Počet dávok/objem *Nr. of doses /volume per container:*	50 vaccine doses / 15 ml
Dátum začiatku platnosti doby exspir/Dátum exspirácie *Date of start of period of validity/Expir.*	7.3.2018 / 6.9.2019
Telefón, fax, e-mail predkladateľa *Contacts*	tel. / fax: +421 37 6533171 mail: bio@pharmagalbio.sk

3 PRODUCTION INFORMATION

Site of manufacture for each antigen (whenever more than one production site exists): **Identical**

3.1 STARTING MATERIALS

3.1.1 Virus seed lots

Master seed material:	**MSV 988M-ca**	**MSV-batch number: 01/04**
Date of last testing:	**ended 29/11/2006**	
Working seed material:	**MSV 988M-ca**	**WSV-batch number: 02/06**
Date of last testing:	**ended 29/11/2006**	

3.1.2. Substrates

3.1.2.1 Eggs for production:

Supplier:	Lohmann	
Flock no.:	20104	20204
Date and results of SPF-testing:	3.10.2017	2.1.2018

3.2 INTERMEDIATE STAGES OF PRODUCTION

Antigen-containing component: Production of Antigen in SPF Embryonated Eggs

3.2.1. *Production of antigen*

Date of inoculation:	30.10.2017	29.1.2018		
Number of embryonated eggs used:	3 657	2 338		
End of production:	3.11.2017	2.2.2018		
Volume of antigen:	33 270 ml	20 930 ml		

3.2.2. *Inactivation*

Start of inactivation: 13.2.2018 End of inactivation: 19.2.2018

Material	*Batch*	*Volume*
Allantoic fluids (Harvest batch No.)	30 10 17	33 200 ml
	29 01 18	20 900 ml
Total volume of allantoic fluid:		54 100 ml
Inactivant - BPL:	A0339642	54,1 ml

3.3. FORMULATION OF THE FINISHED PRODUCT

3.3.1 BLENDING AND VACCINE COMPOSITION

3.3.1.1. Blending of the final bulk (vaccine formulation)

Date of blending: 7.3.2018

Total volume: 100 000 ml

3.3.1.2. Composition of final bulk:

Batch number of the final bulk: 86 03 18

Component	Batch no.	Volume	Target Concentration.	Final Concentration.
Antigen				
PiPMV 988-Ca	13 02 18	27 050 ml	27,0 % ±1 %	27,05%
Adjuvant				
Montanide ISA 763A VG	170127010120	72 750 ml	72,7 % ±1 %	72,75%
Excipients				
Thiomersal 5 % (w/v)	38/18	200 ml	0,2%	0,2%

3.3.2. FILLING

Number of final bulk used for fill: 86 03 18

Final batch No.	Filling date	Quatity of filled containeirs	Volume filled
86 03 18 02	3.8.2018	5 516 pcs	17,5 ml (extractable volume - 15 ml)

3.4. IN PROCESS CONTROLS

3.4.1 In process controls on live viral suspension

Content of haemagglutination units (Code 534-II/2.1)

Date of testing:	3.11.2017	1.2.2018		
Limit of acceptance:	min 64 HAU - max. 256 HAU in 0,05 ml			
Results:	**128**	**64**		
Conclusion:	Complies.	Complies		

Infectious titer EID_{50} (Code 534-II/2.2)

Start of testing:	2.11.2018	5.2.2018		
End of testing:	9.11.2018	12.2.2018		
Limit of acceptance:	min. $10^{8,5}$ EID_{50} - max. $10^{10,2}$ EID_{50} in ml.			
Results:	**$10^{8,62}$ EID_{50}**	**$10^{10,00}$ EID_{50}**		
Conclusion:	Complies.	Complies		

Sterility testing (Code 534-II/2.3)

Start of testing:	3.11.2017	2.2.2018		
End of testing:	17.11.2017	16.2.2018		
Limit of acceptance:	Absence of growth of micro-organisms.			
Results:	**No growth**	**No growth**		
Conclusion:	Complies.	Complies		

3.4.2 In process controls - post- inactivation

Content of HAU in allantoic fluids after inactivation (Code 534-II/2.4)

Date of testing: 22.2.2018

Limits of acceptance: min. 64 HAU - max. 256 HAU in 0,05 ml

Result: **64 HAU in 0,05 ml**

Conclusion: Complies

Control of inactivation (Code 534-II/2.5)

Date of testing: 22.2.2018 - 14.3.2018

Limits of acceptance: Absence of paramyxovirus haemagglutinin in allantoic fluids collected from eggs in the successive passage 3.

Result: **Absence of paramyxovirus haemagglutinin in allantoic fluids collected from eggs in the successive passage 3.**

Conclusion: Complies

3.4.3 In process control - Control of sterility of adjuvant

Sterility testing (Code 534-II/2.6)

Date of testing of the batch: 170127010120 9.3.2018 - 23.3.2018

Limits of acceptance: Absence of growth of microorganisms.

Result: **Absence of growth of microorganisms.**

Conclusion: Complies

4 FINAL TESTING (finished product)

4.1. Finished product in bulk

4.1.1. EXAMINATION OF BIOLOGICAL AND IMMUNOLOGICAL PROPERTIES

Potency (Code 534-III/09)

Date of testing: 28.3.2018 - 19.4.2018

Limits of acceptance: The average value of HI titers must comply with the limits related to the dose applied.

Result:

DOSE APPLIED	AVERAGE HI TITER	LIMIT OF ACCEPTANCE
full vaccine dose	**9,00**	min. 5,81 log_2 - max. 12,31 log_2
1 : 5	**6,40**	min. 4,88 log_2 - max. 10,84 log_2
1 : 10	**5,20**	min. 2,77 log_2 - max. 8,87 log_2

Conclusion: Complies

Identity (Code 534-III/10)

Date of testing: 28.3.2018 - 19.4.2018

Limits of acceptance of results: Formation of specific antibodies to vaccine virus.

Result: **Formation of specific antibodies.**

Conclusion: Complies

Extraneous viruses (Code 534-III/11)

Date of testing: 28.3.2018 - 4.5.2018

Limits of acceptance of results: No presence of extraneous viruses (AEV, IBV, IBDV, ILT, MDV, ALV, EDS, AI).

Result:

RESULTS	AEV	IBV	IBDV	ILT	AI	EDS	MDV	ALV
NEGATIVE	×	×	×	×	×	×	×	×
POSITIVE								

Conclusion: Complies

Inactivation (Code 534-III/12)

Date of testing: 15.3.2018 - 3.4.2018

Limits of acceptance: No signs of Newcastle disease and no virus haemagglutinin must be proved.

Result: **Absence of signs of Newcastle disease and virus haemagglutinin activity.**

Conclusion: Complies

4.1.2. EXAMINATION OF PHYSICOCHEMICAL PROPERTIES

pH value (Code 534-III/13)
Date of testing: 13.3.2018
Limits of acceptance of results: pH 6,5 – 7.5
Result: **pH 6,86**
Conclusion: Complies

Content of thiomersal (Code 534-III/14)
Date of testing: 13.3.2018
Limits of acceptance of results: 0.08 – 0.12 g/l
Result: **0,11 g/l**
Conclusion: Complies

Viscosity (Code 534-III/16)
Date of testing: 29.3.2018
Limits of acceptance of results: 25,7 - 28,5 mPa.s
Result: **28,42 mPa.s**
Conclusion: Complies

4.2. Batch of the finished product

4.2.1. EXAMINATION OF BIOLOGICAL AND IMMUNOLOGICAL PROPERTIES

Sterility testing (Code 534-III/7)
Date of testing of the batch: 9.8.2018 - 23.8.2018
Limits of acceptance: Absence of growth of microorganisms.
Result: **Absence of growth of microorganisms.**
Conclusion: Complies

4.2.2. EXAMINATION OF PHYSICOCHEMICAL PROPERTIES

Appearance (Code 534-III/05)
Date of testing: 9.8.2018
Limits of acceptance: Emulsion of white to light yellow color. Formation of easily shakable sediment is allowed.
Result: **Emulsion of white to light-yellow colour.**
Conclusion: Complies

Extractable volume (Code 534-III/06)

Date of testing: 3.8.2018

Limits of acceptance: 30 vaccine doses (9 ml); 50 vaccine doses (15 ml); 100 vaccine doses (30 ml)

Result: **15 vaccine doses of 0,3 ml each**

Conclusion: Complies

Stability of emulsion (Code 534-III/15)

Date of testing: 9.8.2018

Limits of acceptance of results: Emulsion must be stable.

Results: **Emulsion is stable.**

Conclusion: Complies

5 CERTIFICATION BY THE MANUFACTURER

Certification by qualified person taking the overall responsibility for production and control of the product :

I herewith certify that **COLUMBA Batch 86 03 18 02** was manufactured and tested according to the procedures approved by the competent authorities and complies with the quality requirement and that all measures have been taken to demonstrate compliance with Directive 2001/82/EC as amended by Directive 2009/9/EC.

Name: MVDr. Denisa Svitačová

Function: Head of Quality Control Laboratory (Responsible for Batch Release)

Date: August 23, 2018

Signature:

PHARMAGAL BIO s.r.o.
Murgašova 5
949 01 NITRA