

Manufacturer's Batch Protocol

Product: Bovipast RSP Vakcina A.U.V.

Batch: A096B01

MEMBER STATE SPECIFIC INFORMATION

Member state: **HUNGARY**

Antigen containing component:

Trade name: **Bovipast RSP Vakcina A.U.V.**

Marketing authorisation number:

Target species: **Cattle**

Total number of containers in
this batch: **22 329**

Number of containers the release
is applied for: **22 329**

Number of doses per container: **10**

Number of samples for the
competent authority: **-**

Date of expiry: **Jan-2016**

Name and address of Marketing

Authorisation Holder: **Intervet International B.V.
Wim de Körverstraat 35
5831 AN Boxmeer
THE NETHERLANDS,
represented by the local
company**

15-Dec-2014/as

1103511779/10

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SUMMARY INFORMATION ON THE FINAL BATCH OF FINISHED PRODUCT

Common name of product:	Bovine respiratory syncytial virus, Para-influenza virus and Mannheimia haemolytica vaccine (inactivated) for cattle.
Batch number of finished product:	A096B01
Batch number of final bulk:	A096
Pharmaceutical form of finished product:	Suspension for injection
Type of final container:	Hydrolytical class type I glass
Date of start of period of validity:	22-Jul-2014
Storage temperature:	2-8 °C
Name and address of manufacturer:	Intervet International B.V. Wim de Körverstraat 35 5831 AN BOXMEER NEDERLAND
Name and address of the batch release site:	Intervet International B.V. Wim de Körverstraat 35 5831 AN BOXMEER NEDERLAND

CERTIFICATION BY THE MANUFACTURER

I herewith certify that concerned batch 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.

Name:
Function:
Date:
Signature:

S.T.M. Verstegen
Qualified Person
19 DEC 2014


Manufacturer's Batch Protocol

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Batch: *A096B01*

FINAL BATCH TESTING (FINISHED PRODUCT)

<u>Date on</u>	<u>Date off</u>	<u>Test results</u>
15-Jul-2014	05-Aug-2014	<u>Sterility (1.8)</u> Tested according to Ph. Eur. 0062/Ph.Eur.2.6.1 Result: No growth Threshold: No growth Conclusion: Passed
27-Jun-2014	18-Jul-2014	<u>Inactivation BRSV</u> Result: Inactivated Threshold: Inactivated Conclusion: Passed
27-Jun-2014	18-Jul-2014	<u>Inactivation PI3</u> Result: Inactivated Threshold: Inactivated Conclusion: Passed
19-Sep-2014	10-Oct-2014	<u>Inactivation M. haemolytica</u> Result: Inactivated Threshold: Inactivated Conclusion: Passed
22-Jul-2014	22-Aug-2014	<u>Potency using rabbits (1.6)</u> Result: Conform Threshold: Conform Conclusion: Passed
		<u>BRSV antibody</u> Single result: 45 / 45 / 406 / 199 / 36 / 50 / 128 / 79 / 165 / 285 Average: 144 Result standard: 35 Threshold: Antibody level not sign. lower than std. Conclusion: Passed
		<u>Identity BRSV</u> Result: Identity conform Threshold: Identity conform Conclusion: Passed

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FINAL BATCH TESTING (FINISHED PRODUCT)

<u>Date on</u>	<u>Date off</u>	<u>Test results</u>
		<p><u>PI3 antibody</u></p> <p>Single result: 40 / 40 / 60 / 60 / 100 / 40 / 100 / 40 / 25 / 140 Average: 65 Result standard: 57 Threshold: Antibody level not sign. lower than std. Conclusion: Passed</p> <p><u>Identity PI3</u></p> <p>Result: Identity conform Threshold: Identity conform Conclusion: Passed</p> <p><u>M. haemolytica antibody</u></p> <p>Single result: 47.48 / 57.74 / 79.43 / 91.23 / 62.95 / 67.96 / 69.15 / 60.37 / 47.31 / 67.16 % Average: 65 % Threshold: AB levels not sign. lower than passmark(37.1%) Conclusion: Passed</p> <p><u>M. haemolytica quantification (1.9)</u></p> <p>Single result: 0.397 / 0.399 / 0.627 / 0.408 / 0.377 / 0.427 Average: 0.439 1:5 diluted standard single result: 0.208 / 0.214 / 0.203 / 0.222 / 0.188 / 0.224 Average 1:5 diluted standard: 0.210 Threshold: O.D. significantly > 1:5 diluted std. Conclusion: Passed</p>
25-Jul-2014	25-Jul-2014	<p><u>Aluminium (1.1)</u></p> <p>Tested according to Ph. Eur. 2.5.13 Result: 3 mg/mL Threshold: 2 – 3 mg/mL Conclusion: Passed</p>
01-Sep-2014	01-Sep-2014	<p><u>Formaldehyde (1.2)</u></p> <p>Result: 0.16 mg/mL Threshold: <= 0.50 mg/mL Conclusion: Passed</p>

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FINAL BATCH TESTING (FINISHED PRODUCT)

<u>Date on</u>	<u>Date off</u>	<u>Test results</u>
29-Sep-2014	29-Sep-2014	<u>Sodium timerfonate (1.3)</u> Result: 0.0093 mg/mL Threshold: 0.0085 – 0.0115 mg/mL Conclusion: Passed
24-Jul-2014	24-Jul-2014	<u>pH (1.4)</u> Tested according to Ph. Eur. 2.2.3 Result: 7.8 Threshold: 6.9 – 7.9 Conclusion: Passed
29-Jul-2014	29-Jul-2014	<u>Endotoxin (1.7)</u> Result: 1.6×10^4 IU/dose Threshold: $\leq 2.5 \times 10^5$ IU/dose Conclusion: Passed

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PRODUCTION INFORMATION

<u>Component</u>	<u>Batch</u>	<u>Site(s) of manufacturing</u>
Antigen BRSV	See composition table	Intervet Salamanca, Spain
Antigen PI3	See composition table	Intervet Salamanca, Spain
Antigen M. haemolytica	See composition table	Intervet Milton Keynes, UK
Bulk vaccin	See blending	Intervet Salamanca, Spain
Filled product	see filling	Intervet, Boxmeer, the Netherlands

STARTING MATERIALS:

Virus seed lots:

Master seed material: **BRSV**
MS-batch number: **Lot no. 2, 19.06.1995**
Date of last testing: **27-JUN-1995**

Working seed material: **BRSV**
WS-batch number: **30H10**
Date of last testing: **31-Jan-2011**

Master seed material: **PI3**
MS-batch number: **Lot no. 2, 13.06.1995**
Date of last testing: **27-JUN-1995**

Working seed material: **PI3**
WS-batch number: **12E10**
Date of last testing: **24-Jan-2011**

Bacterial seed lots:

Master seed material: **M. haemolytica**
MS-batch number: **Lot no. S1131/95M, 12-01-1996**
Date of last testing: **26-JAN-1996**

Working seed material: **M. haemolytica**
WS-batch number: **08/10/04/W**
Date of last testing: **26-Jun-2008**

Permanent cell line:

Master cell seed: **MDBK cell line**
MCS-batch number: **6th pas. BW, 25-04-1994**
Date of last testing: **18-JAN-1996**

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INTERMEDIATE STAGES OF PRODUCTION

PRODUCTION OF BRSV COMPONENT:

<u>Production step</u>	<u>Start</u>	<u>End</u>	<u>Volume</u>
Batch SBRS14002			
Seed:	13-Mar-2014	13-Mar-2014	1741.60 m ^l
Harvest:	21-Mar-2014	21-Mar-2014	752.50 kg
Inactivation:	21-Mar-2014	25-Mar-2014	759.50 kg
Batch SBRS14003			
Seed:	20-Mar-2014	20-Mar-2014	1954.70 m ^l
Harvest:	28-Mar-2014	28-Mar-2014	767.50 kg
Inactivation:	28-Mar-2014	01-Apr-2014	774.70 kg

PRODUCTION OF PI3 COMPONENT:

<u>Production step</u>	<u>Start</u>	<u>End</u>	<u>Volume</u>
Batch SPI314002			
Seed:	14-Jan-2014	14-Jan-2014	2927.50 m ^l
Harvest:	20-Jan-2014	20-Jan-2014	917.00 kg
Inactivation:	20-Jan-2014	21-Jan-2014	925.60 kg
Batch SPI314003			
Seed:	28-Jan-2014	28-Jan-2014	2902.40 m ^l
Harvest:	03-Feb-2014	03-Feb-2014	942.00 kg
Inactivation:	03-Feb-2014	04-Feb-2014	950.80 kg

PRODUCTION OF M. HAEMOLYTICA COMPONENT:

<u>Production step</u>	<u>Start</u>	<u>End</u>	<u>Volume</u>
Batch LMHB002702			
Seed:	09-Dec-2013	09-Dec-2013	150.00 L
Harvest:	09-Dec-2013	09-Dec-2013	3000.00 L
Inactivation:	09-Dec-2013	10-Dec-2013	3000.00 L

CREATION OF THE FINISHED PRODUCT

BLENDING OF FINAL BULK:

Batch number:	D435
Start date:	19-Jun-2014
End date:	19-Jun-2014
Total volume:	3000.00 kg

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COMPOSITION OF THE FINAL BULK

Components	Batch no.	Total units
BRSV	SBR14002 SBR14003	752.00 kg
Pi3	SPI314002 SPI314003	600.50 kg
M. haemolytica	LMHB002702	29.10 kg
Adjuvant	SAL14002 SAL14003 SMS1406704	764.86 kg
Excipient	BGM306931 BGM213721 SMS14100 SMS1403802 SMS1406105 SMS1403802	853.54 kg

FILLING

Batch number of final bulk: **A096**
Final batch number: **A096B**
Start date: **07-Jul-2014**
End date: **08-Jul-2014**
Filled containers: **22 329**
Volume filled: **50 ml**

IN PROCESS CONTROLS

In process controls BRSV antigen:

Test	Start	End	Result	Thresholds	Conclusion
Batch SBR14002					
Sterility (before inac)	01-Apr-2014	15-Apr-2014	No growth	No growth	Passed
Antigen content (TCID50)	31-Mar-2014	10-Apr-2014	5.9*	>= 5.4*	Passed
Identity	31-Mar-2014	10-Apr-2014	Conform	Conform	Passed
Sterility (after inac)	02-Apr-2014	16-Apr-2014	No growth	No growth	Passed
Freedom from live virus	28-Mar-2014	02-May-2014	No CPE	No CPE	Passed
pH	25-Mar-2014	25-Mar-2014	7.6	7.2 - 8.2	Passed
* Log10/ml					
Batch SBR14003					
Sterility (before inac)	08-Apr-2014	22-Apr-2014	No growth	No growth	Passed
Antigen content (TCID50)	31-Mar-2014	10-Apr-2014	6.0*	>= 5.4*	Passed
Identity	31-Mar-2014	10-Apr-2014	Conform	Conform	Passed
Sterility (after inac)	08-Apr-2014	22-Apr-2014	No growth	No growth	Passed
Freedom from live virus	04-Apr-2014	16-May-2014	No CPE	No CPE	Passed
pH	01-Apr-2014	01-Apr-2014	7.5	7.2 - 8.2	Passed
* Log10/ml					

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In process controls PI3 antigen:

<u>Test</u>	<u>Start</u>	<u>End</u>	<u>Result</u>	<u>Thresholds</u>	<u>Conclusion</u>
Batch SPI314002					
Sterility (before inac)	21-Jan-2014	04-Feb-2014	No growth	No growth	Passed
Antigen content (TCID50)	10-Feb-2014	20-Feb-2014	7.7*	>= 7.3*	Passed
Identity	10-Feb-2014	20-Feb-2014	Conform	Conform	Passed
Sterility (after inac)	23-Jan-2014	06-Feb-2014	No growth	No growth	Passed
Freedom from live virus	24-Jan-2014	14-Feb-2014	No CPE	No CPE	Passed
pH	21-Jan-2014	21-Jan-2014	7.7	7.2 - 8.2	Passed
* Log10/ml					

Batch SPI314003					
Sterility (before inac)	04-Feb-2014	18-Feb-2014	No growth	No growth	Passed
Antigen content (TCID50)	10-Feb-2014	20-Feb-2014	7.5*	>= 7.3*	Passed
Identity	10-Feb-2014	20-Feb-2014	Conform	Conform	Passed
Sterility (after inac)	06-Feb-2014	20-Feb-2014	No growth	No growth	Passed
Freedom from live virus	07-Feb-2014	28-Feb-2014	No CPE	No CPE	Passed
pH	04-Feb-2014	04-Feb-2014	7.7	7.2 - 8.2	Passed
* Log10/ml					

In process controls M. haemolytica antigen:

<u>Test</u>	<u>Start</u>	<u>End</u>	<u>Result</u>	<u>Thresholds</u>	<u>Conclusion</u>
Batch LMHB002702					
Purity reconstituted WS	07-Dec-2013	08-Dec-2013	Pure	Pure	Passed
Purity primary inoculum	08-Dec-2013	09-Dec-2013	Pure	Pure	Passed
Identity primary inoculum	09-Dec-2013	09-Dec-2013	Conform	Conform	Passed
Purity secondary inoculum	09-Dec-2013	10-Dec-2013	Pure	Pure	Passed
Purity fermenter inoculum	09-Dec-2013	10-Dec-2013	Pure	Pure	Passed
Purity fermenter culture	09-Dec-2013	10-Dec-2013	Pure	Pure	Passed
Iron regulated protein	23-Dec-2013	23-Dec-2013	Present	Present	Passed
Inactivation	10-Dec-2013	31-Dec-2013	No growth	No growth	Passed
Sterility	12-Dec-2013	27-Dec-2013	No growth	No growth	Passed
Formaldehyde	19-Dec-2013	19-Dec-2013	0.82 mg/ml	< 2 mg/ml	Passed
Antigen content	07-Jan-2014	07-Jan-2014	1.88 x 10 ¹¹	* n.a.	Passed
pH	17-Dec-2013	17-Dec-2013	6.6	6.3-7.2	Passed
Specific gravity	17-Dec-2013	17-Dec-2013	1032	N.a.	Passed
* cells/ml					

In process controls final product:

<u>Test</u>	<u>Start</u>	<u>End</u>	<u>Result</u>	<u>Thresholds</u>	<u>Conclusion</u>
Filling volume	07-Jul-2014	08-Jul-2014	52 ml	≥ 51 ml	Passed