

Manufacturer's Batch Protocol

Product: Bovipast RSP Vakcina A.U.V.

Batch: A099A01

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: **22 317**

Number of containers the release
is applied for: **22 317**

Number of doses per container: **10**

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

Date of expiry: **May-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**

27-Mar-2015/RD

1103637346/10

Manufacturer's Batch Protocol

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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:	A099A01
Batch number of final bulk:	A099
Pharmaceutical form of finished product:	Suspension for injection
Type of final container:	Hydrolytical class type I glass
Date of start of period of validity:	28-Nov-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
02 APR 2015


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Batch: A099A01

FINAL BATCH TESTING (FINISHED PRODUCT)

<u>Date on</u>	<u>Date off</u>	<u>Test results</u>
12-Nov-2014	03-Dec-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
07-Nov-2014	28-Nov-2014	<u>Inactivation BRSV</u> Result: Inactivated Threshold: Inactivated Conclusion: Passed
07-Nov-2014	28-Nov-2014	<u>Inactivation PI3</u> Result: Inactivated Threshold: Inactivated Conclusion: Passed
15-Jan-2015	05-Feb-2015	<u>Inactivation M. haemolytica</u> Result: Inactivated Threshold: Inactivated Conclusion: Passed
28-Nov-2014	29-Dec-2014	<u>Potency using rabbits (1.6)</u> Result: Conform Threshold: Conform Conclusion: Passed
		<u>BRSV antibody</u> Single result: 25 / 25 / 88 / 12 / 103 / 181 / 108 / 64 / 99 / 54 Average: 76 Result standard: 12 Threshold: Antibody level not sign. lower than std. Conclusion: Passed

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FINAL BATCH TESTING (FINISHED PRODUCT)

<u>Date on</u>	<u>Date off</u>	<u>Test results</u>
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Identity BRSV

Result: Identity conform
Threshold: Identity conform
Conclusion: Passed

PI3 antibody

Single result: 90 / 60 / 40 / 140 / 40 / 60 / 90 / 20 / 20 / 60
Average: 62
Result standard: 40
Threshold: Antibody level not sign. lower than std.
Conclusion: Passed

Identity PI3

Result: Identity conform
Threshold: Identity conform
Conclusion: Passed

M. haemolytica antibody

Single result: 54.19 / 52.02 / 50.45 / 72.57 / 72.41 / 52.19 / 57.65 / 50.38 / 37.05 / 42.27 %
Average: 54 %
Threshold: AB levels not sign. lower than passmark(37.1%)
Conclusion: Passed

M. haemolytica quantification (1.9)

Single result: 0.421 / 0.414 / 0.408 / 0.425 / 0.407 / 0.364
Average: 0.407
1:5 diluted standard single result: 0.152 / 0.187 / 0.189 / 0.141 / 0.156 / 0.169
Average 1:5 diluted standard: 0.166
Threshold: O.D. significantly > 1:5 diluted std.
Conclusion: Passed

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FINAL BATCH TESTING (FINISHED PRODUCT)

<u>Date on</u>	<u>Date off</u>	<u>Test results</u>
		<u>Aluminium (1.1)</u>
23-Dec-2014	23-Dec-2014	Tested according to Ph. Eur. 2.5.13 Result: 3 mg/mL Threshold: 2 – 3 mg/mL Conclusion: Passed
		<u>Formaldehyde (1.2)</u>
10-Dec-2014	10-Dec-2014	Result: 0.17 mg/mL Threshold: <= 0.50 mg/mL Conclusion: Passed
		<u>Sodium timerfonate (1.3)</u>
23-Dec-2014	23-Dec-2014	Result: 0.0088 mg/mL Threshold: 0.0085 – 0.0115 mg/mL Conclusion: Passed
		<u>pH (1.4)</u>
26-Nov-2014	26-Nov-2014	Tested according to Ph. Eur. 2.2.3 Result: 7.7 Threshold: 6.9 – 7.9 Conclusion: Passed
		<u>Endotoxin (1.7)</u>
27-Nov-2014	27-Nov-2014	Result: 1.9×10^4 IU/dose Threshold: <= 2.5×10^5 IU/dose Conclusion: Passed

**MSD**

Animal Health

Intervet International bv

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Manufacturer's Batch Protocol

*Product: Bovipast RSP Vakcina A.U.V.**Batch: A099A01*

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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Product: Bovipast RSP Vakcina A.U.V.

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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 SBRS140051			
Seed:	09-Jun-2014	09-Jun-2014	1014.00 ml
Harvest:	17-Jun-2014	17-Jun-2014	349.80 kg
Inactivation:	17-Jun-2014	21-Jun-2014	353.10 kg
Batch SBRS140052			
Seed:	09-Jun-2014	09-Jun-2014	1014.00 ml
Harvest:	17-Jun-2014	17-Jun-2014	347.40 kg
Inactivation:	17-Jun-2014	21-Jun-2014	350.60 kg
Batch SBRS140061			
Seed:	16-Jun-2014	16-Jun-2014	1105.00 ml
Harvest:	24-Jun-2014	24-Jun-2014	389.40 kg
Inactivation:	24-Jun-2014	28-Jun-2014	393.00 kg

PRODUCTION OF PI3 COMPONENT:

<u>Production step</u>	<u>Start</u>	<u>End</u>	<u>Volume</u>
Batch SPI314004			
Seed:	12-Feb-2014	12-Feb-2014	3067.00 ml
Harvest:	18-Feb-2014	18-Feb-2014	897.00 kg
Inactivation:	18-Feb-2014	18-Feb-2014	905.40 kg
Batch SPI314005			
Seed:	05-Aug-2014	05-Aug-2014	3662.70 ml
Harvest:	11-Aug-2014	11-Aug-2014	900.00 kg
Inactivation:	11-Aug-2014	12-Aug-2014	908.40 kg

PRODUCTION OF M. HAEMOLYTICA COMPONENT:

<u>Production step</u>	<u>Start</u>	<u>End</u>	<u>Volume</u>
Batch LMHB002802			
Seed:	05-Feb-2014	05-Feb-2014	150.00 L
Harvest:	05-Feb-2014	05-Feb-2014	3000.00 L
Inactivation:	05-Feb-2014	05-Feb-2014	3000.00 L

**MSD**

Animal Health

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msd-animal-health.com**Manufacturer's Batch Protocol***Product: Bovipast RSP Vakcina A.U.V.**Batch: A099A01***CREATION OF THE FINISHED PRODUCT****BLENDING OF FINAL BULK:**Batch number: D577
Start date: 16-Oct-2014
End date: 16-Oct-2014
Total volume: 3000.00 kg**COMPOSITION OF THE FINAL BULK**

Components	Batch no.	Total units
BRSV	SBRS140051	750.50 kg
	SBRS140052	
	SBRS140061	
Pi3	SPI314004	600.10 kg
	SPI314005	
M. haemolytica	LMHB002802	24.50 kg
Adjuvant	SAL14004	764.88 kg
	SMS1414904	
Excipient	SMS14165	860.02 kg
	BGM306931	
	BGM218881	
	SMS1406105	
	SMS1414002	
	SMS1412402	

FILLINGBatch number of final bulk: A099
Final batch number: A099A
Start date: 31-Oct-2014
End date: 31-Oct-2014
Filled containers: 22 317
Volume filled: 50 ml**IN PROCESS CONTROLS****In process controls BRSV antigen:**

Test	Start	End	Result	Thresholds	Conclusion
Batch SBRS140051					
Sterility (before inac)	20-Jun-2014	04-Jul-2014	No growth	No growth	Passed
Antigen content (TCID50)	23-Jun-2014	03-Jul-2014	6.0*	>= 5.4*	Passed
Identity	23-Jun-2014	03-Jul-2014	Conform	Conform	Passed
Sterility (after inac)	26-Jun-2014	10-Jul-2014	No growth	No growth	Passed
Freedom from live virus	27-Jun-2014	18-Jul-2014	No CPE	No CPE	Passed
pH	23-Jun-2014	23-Jun-2014	7.5	7.2 - 8.2	Passed
* Log10/ml					

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Batch: A099A01

In process controls BRSV antigen:

<u>Test</u>	<u>Start</u>	<u>End</u>	<u>Result</u>	<u>Thresholds</u>	<u>Conclusion</u>
Batch SBRS140052					
Sterility (before inac)	20-Jun-2014	04-Jul-2014	No growth	No growth	Passed
Antigen content (TCID50)	23-Jun-2014	03-Jul-2014	5.7*	>= 5.4*	Passed
Identity	23-Jun-2014	03-Jul-2014	Conform	Conform	Passed
Sterility (after inac)	26-Jun-2014	10-Jul-2014	No growth	No growth	Passed
Freedom from live virus	27-Jun-2014	18-Jul-2014	No CPE	No CPE	Passed
pH	23-Jun-2014	23-Jun-2014	7.6	7.2 - 8.2	Passed
* Log10/ml					

Batch SBRS140061					
Sterility (before inac)	27-Jun-2014	11-Jul-2014	No growth	No growth	Passed
Antigen content (TCID50)	14-Jul-2014	24-Jul-2014	6.0*	>= 5.4*	Passed
Identity	30-Jun-2014	10-Jul-2014	Conform	Conform	Passed
Sterility (after inac)	02-Jul-2014	16-Jul-2014	No growth	No growth	Passed
Freedom from live virus	04-Jul-2014	25-Jul-2014	No CPE	No CPE	Passed
pH	30-Jun-2014	30-Jun-2014	7.5	7.2 - 8.2	Passed
* Log10/ml					

In process controls PI3 antigen:

<u>Test</u>	<u>Start</u>	<u>End</u>	<u>Result</u>	<u>Thresholds</u>	<u>Conclusion</u>
Batch SPI314004					
Sterility (before inac)	19-Feb-2014	05-Mar-2014	No growth	No growth	Passed
Antigen content (TCID50)	24-Feb-2014	06-Mar-2014	7.6*	>= 7.3*	Passed
Identity	24-Feb-2014	06-Mar-2014	Conform	Conform	Passed
Sterility (after inac)	25-Feb-2014	11-Mar-2014	No growth	No growth	Passed
Freedom from live virus	21-Feb-2014	14-Mar-2014	No CPE	No CPE	Passed
pH	19-Feb-2014	19-Feb-2014	7.5	7.2 - 8.2	Passed
* Log10/ml					

Batch SPI314005					
Sterility (before inac)	13-Aug-2014	27-Aug-2014	No growth	No growth	Passed
Antigen content (TCID50)	18-Aug-2014	28-Aug-2014	7.6*	>= 7.3*	Passed
Identity	18-Aug-2014	28-Aug-2014	Conform	Conform	Passed
Sterility (after inac)	14-Aug-2014	28-Aug-2014	No growth	No growth	Passed
Freedom from live virus	22-Aug-2014	19-Sep-2014	No CPE	No CPE	Passed
pH	12-Aug-2014	12-Aug-2014	7.7	7.2 - 8.2	Passed
* Log10/ml					



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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 LMHB002802					
Purity reconstituted WS	03-Feb-2014	04-Feb-2014	Pure	Pure	Passed
Purity primary inoculum	04-Feb-2014	05-Feb-2014	Pure	Pure	Passed
Identity primary inoculum	06-Feb-2014	06-Feb-2014	Conform	Conform	Passed
Purity secondary inoculum	05-Feb-2014	06-Feb-2014	Pure	Pure	Passed
Purity fermentor inoculum	05-Feb-2014	06-Feb-2014	Pure	Pure	Passed
Purity fermentor culture	05-Feb-2014	06-Feb-2014	Pure	Pure	Passed
Iron regulated protein	13-Feb-2014	13-Feb-2014	Present	Present	Passed
Inactivation	06-Feb-2014	27-Feb-2014	No growth	No growth	Passed
Sterility	11-Feb-2014	25-Feb-2014	No growth	No growth	Passed
Formaldehyde	10-Feb-2014	10-Feb-2014	1.3 mg/ml	< 2 mg/ml	Passed
Antigen content	14-Mar-2014	14-Mar-2014	2.23 x 10 ¹¹	* n.a.	Passed
pH	10-Feb-2014	10-Feb-2014	6.7	6.3-7.2	Passed
Specific gravity	10-Feb-2014	10-Feb-2014	1033	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	31-Oct-2014	31-Oct-2014	52 ml	≥ 51 ml	Passed