

Manufacturer's Batch Protocol

Product: Bovipast RSP Vakcina A.U.V.

Batch: A094A01

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:

10 925

Number of containers the release
is applied for:

10 925

Number of doses per container:

10

Number of samples for the
competent authority:

-

Date of expiry:

Dec-2015

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**

24-Oct-2014/s1

1103428739/10

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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:	A094A01
Batch number of final bulk:	A094
Pharmaceutical form of finished product:	Suspension for injection
Type of final container:	Hydrolytical class type I glass
Date of start of period of validity:	24-Jun-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:

P.G. Mooren Qualified Person 29 OCT 2014 

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FINAL BATCH TESTING (FINISHED PRODUCT)

<u>Date on</u>	<u>Date off</u>	<u>Test results</u>
20-Jun-2014	11-Jul-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
06-Jun-2014	04-Jul-2014	<u>Inactivation BRSV</u> Result: Inactivated Threshold: Inactivated Conclusion: Passed
06-Jun-2014	04-Jul-2014	<u>Inactivation PI3</u> Result: Inactivated Threshold: Inactivated Conclusion: Passed
03-Jul-2014	24-Jul-2014	<u>Inactivation M. haemolytica</u> Result: Inactivated Threshold: Inactivated Conclusion: Passed
24-Jun-2014	25-Jul-2014	<u>Potency using rabbits (1.6)</u> Result: Conform Threshold: Conform Conclusion: Passed
		<u>BRSV antibody</u> Single result: 83 / 32 / 6 / 70 / 76 / 285 / 54 / 169 / 279 / 47 Average: 110 Result standard: 45 Threshold: Antibody level not sign. lower than std. Conclusion: Passed

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FINAL BATCH TESTING (FINISHED PRODUCT)

Date on Date off Test results

Identity BRSV

Result: Identity conform
Threshold: Identity conform
Conclusion: Passed

PI3 antibody

Single result: 60 / 80 / 60 / 40 / 120 / 180 / 20 / 50 / 80 / 160
Average: 85
Result standard: 60
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: 67.68 / 62.96 / 58.26 / 60.54 / 62.42 / 80.81 / 54.10 / 66.47 / 78.60 / 83.17 %
Average: 68 %
Threshold: AB levels not sign. lower than passmark(37.1%)
Conclusion: Passed

M. haemolytica quantification (1.9)

Single result: 0.465 / 0.393 / 0.424 / 0.451 / 0.427 / 0.450
Average: 0.435
1:5 diluted standard single result: 0.134 / 0.161 / 0.148 / 0.164 / 0.116 / 0.140
Average 1:5 diluted standard: 0.144
Threshold: O.D. significantly > 1:5 diluted std.
Conclusion: Passed

Aluminium (1.1)

25-Jul-2014 25-Jul-2014 Tested according to Ph. Eur. 2.5.13
Result: 3 mg/mL
Threshold: 2 – 3 mg/mL
Conclusion: Passed

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FINAL BATCH TESTING (FINISHED PRODUCT)

<u>Date on</u>	<u>Date off</u>	<u>Test results</u>
24-Jun-2014	24-Jun-2014	<u>Formaldehyde (1.2)</u> Result: 0.17 mg/mL Threshold: <= 0.50 mg/mL Conclusion: Passed
15-Jul-2014	15-Jul-2014	<u>Sodium timerfonate (1.3)</u> Result: 0.0092 mg/mL Threshold: 0.0085 – 0.0115 mg/mL Conclusion: Passed
30-Jun-2014	30-Jun-2014	<u>pH (1.4)</u> Tested according to Ph. Eur. 2.2.3 Result: 7.9 Threshold: 6.9 – 7.9 Conclusion: Passed
03-Jul-2014	03-Jul-2014	<u>Endotoxin (1.7)</u> Result: 1.8×10^4 IU/dose Threshold: <= 2.5×10^5 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 SBRS13012			
Seed:	12-Sep-2013	12-Sep-2013	1996.00 m ^l
Harvest:	20-Sep-2013	20-Sep-2013	779.50 kg
Inactivation:	20-Sep-2013	24-Sep-2013	786.80 kg
Batch SBRS13013			
Seed:	19-Sep-2013	19-Sep-2013	2093.00 m ^l
Harvest:	27-Sep-2013	27-Sep-2013	788.50 kg
Inactivation:	27-Sep-2013	01-Oct-2013	795.90 kg
Batch SBRS14001			
Seed:	06-Mar-2014	06-Mar-2014	2167.60 m ^l
Harvest:	14-Mar-2014	14-Mar-2014	700.50 kg
Inactivation:	14-Mar-2014	18-Mar-2014	707.00 kg

PRODUCTION OF PI3 COMPONENT:

<u>Production step</u>	<u>Start</u>	<u>End</u>	<u>Volume</u>
Batch SPI313007			
Seed:	06-Aug-2013	06-Aug-2013	2903.70 m ^l
Harvest:	12-Aug-2013	12-Aug-2013	892.40 kg
Inactivation:	12-Aug-2013	13-Aug-2013	900.80 kg
Batch SPI314001			
Seed:	31-Dec-2013	31-Dec-2013	2933.00 m ^l
Harvest:	06-Jan-2014	06-Jan-2014	895.60 kg
Inactivation:	06-Jan-2014	07-Jan-2014	904.00 kg
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

PRODUCTION OF M. HAEMOLYTICA COMPONENT:

<u>Production step</u>	<u>Start</u>	<u>End</u>	<u>Volume</u>
Batch LMHB002602			
Seed:	24-Sep-2013	24-Sep-2013	150.00 L
Harvest:	24-Sep-2013	24-Sep-2013	3000.00 L
Inactivation:	24-Sep-2013	25-Sep-2013	3000.00 L
Batch LMHB002701			
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

Manufacturer's Batch Protocol

Product: Bovipast RSP Vakcina A.U.V.

Batch: A094A01

CREATION OF THE FINISHED PRODUCT

BLENDING OF FINAL BULK:

Batch number: **A094**
Start date: **22-May-2014**
End date: **22-May-2014**
Total volume: **3000.00 kg**

COMPOSITION OF THE FINAL BULK

Components	Batch no.	Total units
BRSV	SBRS13012, SBRS13013, SBRS14001	751.00 kg
Pi3	SPI313007, SPI314001, SPI314002	601.06 kg
M. haemolytica	LMHB002701, LMHB002602	29.88 kg
Adjuvant	SAL14001, SAL14002, SMS1406204	764.86 kg
Excipient	SMS14089, BMGM306931, BMGM213721, SMS1401705, SMS1403802	853.20 kg

FILLING

Batch number of final bulk: **A094**
Final batch number: **A094A**
Start date: **11-Jun-2014**
End date: **12-Jun-2014**
Filled containers: **10 925**
Volume filled: **50 ml**

IN PROCESS CONTROLS

In process controls BRSV antigen:

<u>Test</u>	<u>Start</u>	<u>End</u>	<u>Result</u>	<u>Thresholds</u>	<u>Conclusion</u>
Batch SBRS13012					
Sterility (before inac)	25-Sep-2013	09-Oct-2013	No growth	No growth	Passed
Antigen content (TCID50)	04-Oct-2013	14-Oct-2013	5.9*	>= 5.4*	Passed
Identity	04-Oct-2013	14-Oct-2013	Conform	Conform	Passed
Sterility (after inac)	27-Sep-2013	11-Oct-2013	No growth	No growth	Passed
Freedom from live virus	27-Sep-2013	18-Oct-2013	No CPE	No CPE	Passed
pH	25-Sep-2013	25-Sep-2013	7.5	7.2 - 8.2	Passed
* Log10/ml					

Manufacturer's Batch Protocol

Product: Bovipast RSP Vakcina A.U.V.

Batch: A094A01

In process controls BRSV antigen:

<u>Test</u>	<u>Start</u>	<u>End</u>	<u>Result</u>	<u>Thresholds</u>	<u>Conclusion</u>
Batch SBRS13013					
Sterility (before inac)	02-Oct-2013	16-Oct-2013	No growth	No growth	Passed
Antigen content (TCID50)	04-Oct-2013	14-Oct-2013	5.8*	>= 5.4*	Passed
Identity	04-Oct-2013	14-Oct-2013	Conform	Conform	Passed
Sterility (after inac)	04-Oct-2013	18-Oct-2013	No growth	No growth	Passed
Freedom from live virus	04-Oct-2013	25-Oct-2013	No CPE	No CPE	Passed
pH TK1	02-Sep-2013	02-Sep-2013	7.3	7.2 - 8.2	Passed
pH TK2	02-Sep-2013	02-Sep-2013	7.4	7.2 - 8.2	Passed
* Log10/ml					

Batch SBRS14001

Sterility (before inac)	18-Mar-2014	01-Apr-2014	No growth	No growth	Passed
Antigen content (TCID50)	21-Mar-2014	31-Mar-2014	5.7*	>= 5.4*	Passed
Identity	21-Mar-2014	31-Mar-2014	Conform	Conform	Passed
Sterility (after inac)	21-Mar-2014	04-Apr-2014	No growth	No growth	Passed
Freedom from live virus	21-Mar-2014	11-Apr-2014	No CPE	No CPE	Passed
pH	18-Mar-2014	18-Mar-2014	7.7	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 SPI313007					
Sterility (before inac)	13-Aug-2013	27-Aug-2013	No growth	No growth	Passed
Antigen content (TCID50)	02-Sep-2013	12-Sep-2013	8.4*	>= 7.3*	Passed
Identity	19-Aug-2013	29-Aug-2013	Conform	Conform	Passed
Sterility (after inac)	14-Aug-2013	28-Aug-2013	No growth	No growth	Passed
Freedom from live virus	16-Aug-2013	13-Sep-2013	No CPE	No CPE	Passed
pH	13-Aug-2013	13-Aug-2013	7.6	7.2 - 8.2	Passed
* Log10/ml					

Batch SPI314001

Sterility (before inac)	08-Jan-2014	22-Jan-2014	No growth	No growth	Passed
Antigen content (TCID50)	13-Jan-2014	23-Jan-2014	7.8*	>= 7.3*	Passed
Identity	13-Jan-2014	23-Jan-2014	Conform	Conform	Passed
Sterility (after inac)	09-Jan-2014	23-Jan-2014	No growth	No growth	Passed
Freedom from live virus	10-Jan-2014	31-Jan-2014	No CPE	No CPE	Passed
pH	07-Jan-2014	07-Jan-2014	7.7	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					

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 LMHB002602					
Purity reconstituted WS	22-Sep-2013	23-Sep-2013	Pure	Pure	Passed
Purity primary inoculum	23-Sep-2013	24-Sep-2013	Pure	Pure	Passed
Identity primary inoculum	25-Sep-2013	25-Sep-2013	Conform	Conform	Passed
Purity secondary inoculum	24-Sep-2013	25-Sep-2013	Pure	Pure	Passed
Purity fermentor inoculum	24-Sep-2013	25-Sep-2013	Pure	Pure	Passed
Purity fermentor culture	24-Sep-2013	25-Sep-2013	Pure	Pure	Passed
Iron regulated protein	27-Sep-2013	27-Sep-2013	Present	Present	Passed
Inactivation	25-Sep-2013	16-Oct-2013	No growth	No growth	Passed
Sterility	27-Sep-2013	11-Oct-2013	No growth	No growth	Passed
Formaldehyde	01-Oct-2013	01-Oct-2013	1.07 mg/ml	< 2 mg/ml	Passed
Antigen content	07-Oct-2013	07-Oct-2013	1.73 x 10 ¹¹ *	n.a.	Passed
pH	02-Oct-2013	02-Oct-2013	6.7	6.3-7.2	Passed
Specific gravity	02-Oct-2013	02-Oct-2013	1032	N.a.	Passed
* cells/ml					
Batch LMHB002701					
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	1.95 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					

Manufacturer's Batch Protocol

Product: Bovipast RSP Vakcina A.U.V.

Batch: A094A01

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	11-Jun-2014	12-Jun-2014	52 ml	≥ 51 ml	Passed