

## Manufacturer's Batch Protocol

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

*Batch: A091B02*

### 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:

**22 342**

Number of containers the release  
is applied for:

**22 342**

Number of doses per container:

**10**

Number of samples for the  
competent authority:

**-**

Date of expiry:

**Nov-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**

**15-Sep-2014/mw**

**1103376677/10**

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### SUMMARY INFORMATION ON THE FINAL BATCH OF FINISHED PRODUCT

Common name of product:	<b>Bovine respiratory syncytial virus, Para-influenza virus and Mannheimia haemolytica vaccine (inactivated) for cattle.</b>
Batch number of finished product:	<b>A091B02</b>
Batch number of final bulk:	<b>A091</b>
Pharmaceutical form of finished product:	<b>Suspension for injection</b>
Type of final container:	<b>Hydrolytical class type I glass</b>
Date of start of period of validity:	<b>05-May-2014</b>
Storage temperature:	<b>2-8 °C</b>
Name and address of manufacturer:	<b>Intervet International B.V. Wim de Körverstraat 35 5831 AN BOXMEER NEDERLAND</b>
Name and address of the batch release site:	<b>Intervet International B.V. Wim de Körverstraat 35 5831 AN BOXMEER NEDERLAND</b>

### 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:	<b>P.G. Mooren</b>
Function:	<b>Qualified Person</b>
Date:	<b>18 SEP 2014</b>
Signature:	

## Manufacturer's Batch Protocol

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Batch: *A091B02*

### FINAL BATCH TESTING (FINISHED PRODUCT)

<u>Date on</u>	<u>Date off</u>	<u>Test results</u>
10-Apr-2014	01-May-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
28-Mar-2014	02-May-2014	<u>Inactivation BRSV</u> Result: Inactivated Threshold: Inactivated Conclusion: Passed
28-Mar-2014	02-May-2014	<u>Inactivation PI3</u> Result: Inactivated Threshold: Inactivated Conclusion: Passed
01-May-2014	22-May-2014	<u>Inactivation M. haemolytica</u> Result: Inactivated Threshold: Inactivated Conclusion: Passed
05-May-2014	05-Jun-2014	<u>Potency using rabbits (1.6)</u> Result: Conform Threshold: Conform Conclusion: Passed
		<u>BRSV antibody</u> Single result: 398 / 57 / 57 / 45 / 64 / 23 / 91 / 206 / 58 / 49 Average: 105 Result standard: 15 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)

Date on      Date off      Test results

#### PI3 antibody

Single result: 100 / 90 / 100 / 120 / 60 / 60 /  
80 / 140 / 200 / 320

Average: 127

Result standard: 53

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: 72.12 / 65.10 / 65.28 / 74.91 / 74.57 / 56.68  
/ 62.49 / 67.70 / 50.06 / 77.77 %

Average: 67 %

Threshold: AB levels not sign. lower than passmark(37.1%)

Conclusion: Passed

#### M. haemolytica quantification (1.9)

Single result: 0.474 / 0.551 / 0.559 / 0.526 / 0.489 / 0.540

Average: 0.523

1:5 diluted standard single result:

0.124 / 0.121 / 0.102 / 0.130 / 0.127 / 0.114

Average 1:5 diluted standard: 0.120

Threshold: O.D. significantly > 1:5 diluted std.

Conclusion: Passed

#### Aluminium (1.1)

05-May-2014    05-May-2014    Tested according to Ph. Eur. 2.5.13

Result: 3 mg/mL

Threshold: 2 – 3 mg/mL

Conclusion: Passed

#### Formaldehyde (1.2)

24-Jun-2014    24-Jun-2014

Result: 0.16 mg/mL

Threshold: <= 0.50 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>
22-Apr-2014	22-Apr-2014	<u>Sodium timerfonate (1.3)</u> Result: 0.0092 mg/mL Threshold: 0.0085 – 0.0115 mg/mL Conclusion: Passed
22-Apr-2014	22-Apr-2014	<u>pH (1.4)</u> Tested according to Ph. Eur. 2.2.3 Result: 7.9 Threshold: 6.9 – 7.9 Conclusion: Passed
14-Apr-2014	14-Apr-2014	<u>Endotoxin (1.7)</u> Result: $1.8 \times 10^4$ 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: **6<sup>th</sup> 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 SBRS13011			
Seed:	05-Sep-2013	05-Sep-2013	2277.00 m <sup>l</sup>
Harvest:	13-Sep-2013	13-Sep-2013	733.50 kg
Inactivation:	13-Sep-2013	17-Sep-2013	740.40 kg
Batch SBRS13013			
Seed:	19-Sep-2013	19-Sep-2013	2093.00 m <sup>l</sup>
Harvest:	27-Sep-2013	27-Sep-2013	788.50 kg
Inactivation:	27-Sep-2013	01-Oct-2013	795.90 kg

#### PRODUCTION OF PI3 COMPONENT:

<u>Production step</u>	<u>Start</u>	<u>End</u>	<u>Volume</u>
Batch SPI313006			
Seed:	23-Jul-2013	23-Jul-2013	3200.00 m <sup>l</sup>
Harvest:	29-Jul-2013	29-Jul-2013	841.40 kg
Inactivation:	29-Jul-2013	30-Jul-2013	849.30 kg
Batch SPI313007			
Seed:	06-Aug-2013	06-Aug-2013	2903.70 m <sup>l</sup>
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 <sup>l</sup>
Harvest:	06-Jan-2014	06-Jan-2014	895.60 kg
Inactivation:	06-Jan-2014	07-Jan-2014	904.00 kg

#### PRODUCTION OF M. HAEMOLYTICA COMPONENT:

<u>Production step</u>	<u>Start</u>	<u>End</u>	<u>Volume</u>
Batch LMHB002601			
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

### CREATION OF THE FINISHED PRODUCT

#### BLENDING OF FINAL BULK:

Batch number: D331  
Start date: 20-Mar-2014  
End date: 20-Mar-2014  
Total volume: 3000.00 kg

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*Batch: A091B02*

### COMPOSITION OF THE FINAL BULK

Components	Batch no.	Total units
BRSV	SBRS13011 SBRS13013	750.04 kg
Pi3	SPI313006 SPI313007 SPI314001	600.50 kg
M. haemolytica	LMHB002601	31.20 kg
Adjuvant	SMS1402904 SAL13005 SAL14001	764.88 kg
Excipient	SMS1401705 SMS14040 BMGM213721 BMGM306931	853.38 kg

### FILLING

Batch number of final bulk: **A091**  
Final batch number: **A091B**  
Start date: **01-Apr-2014**  
End date: **02-Apr-2014**  
Filled containers: **22 342**  
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 SBRS13011					
Sterility (before inac)	18-Sep-2013	02-Oct-2013	No growth	No growth	Passed
Antigen content (TCID50)	20-Sep-2013	30-Sep-2013	6.3*	>= 5.4*	Passed
Identity	20-Sep-2013	30-Sep-2013	Conform	Conform	Passed
Sterility (after inac)	20-Sep-2013	04-Oct-2013	No growth	No growth	Passed
Freedom from live virus	20-Sep-2013	11-Oct-2013	No CPE	No CPE	Passed
pH	18-Sep-2013	18-Sep-2013	7.6	7.2 - 8.2	Passed
* Log10/ml					
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					



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*Batch: A091B02*

### In process controls PI3 antigen:

<u>Test</u>	<u>Start</u>	<u>End</u>	<u>Result</u>	<u>Thresholds</u>	<u>Conclusion</u>
Batch SPI313006					
Sterility (before inac)	30-Jul-2013	13-Aug-2013	No growth	No growth	Passed
Antigen content (TCID50)	02-Sep-2013	12-Sep-2013	8.3*	>= 7.3*	Passed
Identity	19-Aug-2013	29-Aug-2013	Conform	Conform	Passed
Sterility (after inac)	01-Aug-2013	15-Aug-2013	No growth	No growth	Passed
Freedom from live virus	02-Aug-2013	23-Aug-2013	No CPE	No CPE	Passed
pH	30-Jul-2013	30-Jul-2013	7.7	7.2 - 8.2	Passed
* Log10/ml					

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					

### In process controls M. haemolytica antigen:

Batch LMHB002601					
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 mg/ml	< 2 mg/ml	Passed
Antigen content	06-Nov-2013	06-Nov-2013	1.75 x 10 <sup>11</sup> *	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					

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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	01-Apr-2014	02-Apr-2014	52 ml	≥ 51 ml	Passed