

## Manufacturer's Batch Protocol

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

*Batch: A086A02*

### 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:

**18 722**

Number of containers the release  
is applied for:

**18 722**

Number of doses per container:

**10**

Number of samples for the  
competent authority:

**-**

Date of expiry:

**May-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**

**02-Apr-2014/cc**

**1103149459/10**

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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>A086A02</b>
Batch number of final bulk:	<b>A086</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>11-Nov-2013</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:  
Function:  
Date:  
Signature: .....

**S.T.M. Verstegen**  
Qualified Person  
**11 APR 2014**  


## Manufacturer's Batch Protocol

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### FINAL BATCH TESTING (FINISHED PRODUCT)

<u>Date on</u>	<u>Date off</u>	<u>Test results</u>
16-Oct-2013	06-Nov-2013	<p><b><u>Sterility (1.8)</u></b> Tested according to Ph. Eur. 0062/Ph.Eur.2.6.1 Result: No growth Threshold: No growth Conclusion: Passed</p>
27-Sep-2013	18-Oct-2013	<p><b><u>Inactivation BRSV</u></b> Result: Inactivated Threshold: Inactivated Conclusion: Passed</p>
27-Sep-2013	18-Oct-2013	<p><b><u>Inactivation PI3</u></b> Result: Inactivated Threshold: Inactivated Conclusion: Passed</p>
03-Oct-2013	24-Oct-2013	<p><b><u>Inactivation M. haemolytica</u></b> Result: Inactivated Threshold: Inactivated Conclusion: Passed</p>
11-Nov-2013	12-Dec-2013	<p><b><u>Potency using rabbits (1.6)</u></b> Result: Conform Threshold: Conform Conclusion: Passed</p> <p><b><u>BRSV antibody</u></b></p> <p>Single result: 79 / 91 / 15 / 152 / 76 / 26 / 50 / 54 / 169 / 41 Average: 75 Result standard: 20 Threshold: Antibody level not sign. lower than std. Conclusion: Passed</p> <p><b><u>Identity BRSV</u></b> Result: Identity conform Threshold: Identity conform Conclusion: Passed</p>

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### FINAL BATCH TESTING (FINISHED PRODUCT)

Date on      Date off      Test results

#### PI3 antibody

Single result: 160 / 40 / 320 / 180 / 80 / 180 / 80 / 160 / 160 / 240

Average: 160

Result standard: 80

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: 54.88 / 56.92 / 51.41 / 53.30 / 26.59 / 65.38 / 66.57 / 68.62 / 62.43 / 51.06 %

Average: 56 %

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

Conclusion: Passed

#### M. haemolytica quantification (1.9)

Single result: 0.258 / 0.224 / 0.339 / 0.256 / 0.301 / 0.278

Average: 0.276

1:5 diluted standard single result: 0.075 / 0.076 / 0.080 / 0.074 / 0.091 / 0.074

Average 1:5 diluted standard: 0.078

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

Conclusion: Passed

#### Aluminium (1.1)

18-Nov-2013    18-Nov-2013    Tested according to Ph. Eur. 2.5.13

Result: 3 mg/mL

Threshold: 2 – 3 mg/mL

Conclusion: Passed

#### Formaldehyde (1.2)

04-Nov-2013    04-Nov-2013

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>
02-Dec-2013	02-Dec-2013	<u>Sodium timerfonate (1.3)</u> Result: 0.0094 mg/mL Threshold: 0.0085 – 0.0115 mg/mL Conclusion: Passed
25-Oct-2013	25-Oct-2013	<u>pH (1.4)</u> Tested according to Ph. Eur. 2.2.3 Result: 7.8 Threshold: 6.9 – 7.9 Conclusion: Passed
12-Nov-2013	12-Nov-2013	<u>Endotoxin (1.7)</u> Result: $1.9 \times 10^4$ 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 composition table	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: 03-Feb-2005

#### 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 SBRS13004			
Seed:	18-Feb-2013	18-Feb-2013	1853.00 m <sup>l</sup>
Harvest:	26-Feb-2013	26-Feb-2013	766.00 kg
Inactivation:	26-Feb-2013	02-Mar-2013	773.20 kg
Batch SBRS13005			
Seed:	25-Feb-2013	25-Feb-2013	2149.00 m <sup>l</sup>
Harvest:	05-Mar-2013	05-Mar-2013	771.50 kg
Inactivation:	05-Mar-2013	09-Mar-2013	778.70 kg

#### PRODUCTION OF PI3 COMPONENT:

<u>Production step</u>	<u>Start</u>	<u>End</u>	<u>Volume</u>
Batch SPI313003			
Seed:	06-Feb-2013	06-Feb-2013	3309.00 m <sup>l</sup>
Harvest:	12-Feb-2013	12-Feb-2013	904.20 kg
Inactivation:	12-Feb-2013	13-Feb-2013	912.70 kg
Batch SPI313004			
Seed:	20-Feb-2013	20-Feb-2013	3384.00 m <sup>l</sup>
Harvest:	26-Feb-2013	26-Feb-2013	897.60 kg
Inactivation:	26-Feb-2013	27-Feb-2013	906.00 kg

#### PRODUCTION OF M. HAEMOLYTICA COMPONENT:

<u>Production step</u>	<u>Start</u>	<u>End</u>	<u>Volume</u>
Batch LMHB002302			
Seed:	21-Feb-2013	21-Feb-2013	150 L
Harvest:	21-Feb-2013	21-Feb-2013	3000 L
Inactivation:	21-Feb-2013	22-Feb-2013	3000 L
Batch LMHB002401			
Seed:	07-May-2013	07-May-2013	150 L
Harvest:	07-May-2013	07-May-2013	3000 L
Inactivation:	07-May-2013	08-May-2013	3000 L

### CREATION OF THE FINISHED PRODUCT

#### BLENDING OF FINAL BULK:

Batch number: **D122**  
Start date: **12-Sep-2013**  
End date: **12-Sep-2013**  
Total volume: **3000.00 kg**

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### COMPOSITION OF THE FINAL BULK

Components	Batch no.	Total units
BRSV	SBR13004, SBR13005	750.78 kg
Pi3	SPI13003, SPI13004	600.50 kg
M. haemolytica	LMHB002302, LMHB002401	37.00 kg
Adjuvant	SAL13002, SMS1311504	764.88 kg
Excipient	SMS13130, BMGM306931, BMGM213721, SMS1304805, SMS1309302,	846.84 kg

### FILLING

Batch number of final bulk: **A086**  
Final batch number: **A086A**  
Start date: **08-Oct-2013**  
End date: **08-Oct-2013**  
Filled containers: **18 722**  
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 SBR13004					
Cell controls:					
Microscopic inspection	15-Feb-2013	01-Mar-2013	No CPE	No CPE	Passed
Haemadsorption	01-Mar-2013	01-Mar-2013	No haemads.	No haemads.	Passed
Passage in vero cells	06-Mar-2013	20-Mar-2013	No CPE	No CPE	Passed
Sterility (before inac)	01-Mar-2013	15-Mar-2013	No growth	No growth	Passed
Antigen content (TCID50)	11-Mar-2013	21-Mar-2013	6.0*	>= 5.4*	Passed
Identity	11-Mar-2013	21-Mar-2013	Conform	Conform	Passed
Sterility (after inac)	06-Mar-2013	20-Mar-2013	No growth	No growth	Passed
Freedom from live virus	15-Mar-2013	11-May-2013	No CPE	No CPE	Passed
pH	04-Mar-2013	04-Mar-2013	7.6	7.2 - 8.2	Passed
* Log10/ml					

#### Batch SBR13005

##### Cell controls:

Microscopic inspection	22-Feb-2013	08-Mar-2013	No CPE	No CPE	Passed
Haemadsorption	08-Mar-2013	08-Mar-2013	No haemads.	No haemads.	Passed
Passage in vero cells	12-Mar-2013	26-Mar-2013	No CPE	No CPE	Passed
Sterility (before inac)	08-Mar-2013	22-Mar-2013	No growth	No growth	Passed
Antigen content (TCID50)	11-Mar-2013	21-Mar-2013	5.8*	>= 5.4*	Passed
Identity	11-Mar-2013	21-Mar-2013	Conform	Conform	Passed
Sterility (after inac)	13-Mar-2013	27-Mar-2013	No growth	No growth	Passed
Freedom from live virus	15-Mar-2013	11-May-2013	No CPE	No CPE	Passed
pH	11-Mar-2013	11-Mar-2013	7.4	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 SPI313003					
Cell controls:					
Microscopic inspection	01-Feb-2013	15-Feb-2013	No CPE	No CPE	Passed
Haemadsorption	15-Feb-2013	15-Feb-2013	No haemads.	No haemads.	Passed
Passage in vero cells	19-Feb-2013	05-Mar-2013	No CPE	No CPE	Passed
Sterility (before inac)	14-Feb-2013	28-Feb-2013	No growth	No growth	Passed
Antigen content (TCID50)	04-Mar-2013	14-Mar-2013	8.3*	>= 7.3*	Passed
Identity	04-Mar-2013	14-Mar-2013	Conform	Conform	Passed
Sterility (after inac)	15-Feb-2013	01-Mar-2013	No growth	No growth	Passed
Freedom from live virus	01-Mar-2013	22-Mar-2013	No CPE	No CPE	Passed
pH	13-Feb-2013	13-Feb-2013	7.7	7.2 - 8.2	Passed
* Log10/ml					

### Batch SPI313004

#### Cell controls:

Microscopic inspection	15-Feb-2013	01-Mar-2013	No CPE	No CPE	Passed
Haemadsorption	01-Mar-2013	01-Mar-2013	No haemads.	No haemads.	Passed
Passage in vero cells	06-Mar-2013	20-Mar-2013	No CPE	No CPE	Passed
Sterility (before inac)	28-Feb-2013	14-Mar-2013	No growth	No growth	Passed
Antigen content (TCID50)	04-Mar-2013	14-Mar-2013	7.9*	>= 7.3*	Passed
Identity	04-Mar-2013	14-Mar-2013	Conform	Conform	Passed
Sterility (after inac)	28-Feb-2013	14-Mar-2013	No growth	No growth	Passed
Freedom from live virus	01-Mar-2013	12-Apr-2013	No CPE	No CPE	Passed
pH	27-Feb-2013	27-Feb-2013	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 LMHB002302					
Purity reconstituted WS	19-Feb-2013	20-Feb-2013	Pure	Pure	Passed
Purity primary inoculum	20-Feb-2013	21-Feb-2013	Pure	Pure	Passed
Identity primary inoculum	22-Feb-2013	22-Feb-2013	Conform	Conform	Passed
Purity secondary inoculum	21-Feb-2013	22-Feb-2013	Pure	Pure	Passed
Purity fermentor inoculum	21-Feb-2013	22-Feb-2013	Pure	Pure	Passed
Purity fermentor culture	21-Feb-2013	22-Feb-2013	Pure	Pure	Passed
Iron regulated protein	19-Mar-2013	19-Mar-2013	Present	Present	Passed
Inactivation	22-Feb-2013	15-Mar-2013	No growth	No growth	Passed
Sterility	01-Mar-2013	15-Mar-2013	No growth	No growth	Passed
Formaldehyde	27-Feb-2013	27-Feb-2013	1.4 mg/ml	< 2 mg/ml	Passed
Antigen content	19-Mar-2013	19-Mar-2013	1.63 x 10 <sup>11</sup> *	n.a.	Passed
pH	01-Mar-2013	01-Mar-2013	6.6	6.3-7.2	Passed
Specific gravity	01-Mar-2013	01-Mar-2013	1033	N.a.	Passed
* cells/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 LMHB002401					
Purity reconstituted WS	05-May-2013	06-May-2013	Pure	Pure	Passed
Purity primary inoculum	05-May-2013	06-May-2013	Pure	Pure	Passed
Identity primary inoculum	08-May-2013	08-May-2013	Conform	Conform	Passed
Purity secondary inoculum	06-May-2013	07-May-2013	Pure	Pure	Passed
Purity fermentor inoculum	07-May-2013	08-May-2013	Pure	Pure	Passed
Purity fermentor culture	07-May-2013	08-May-2013	Pure	Pure	Passed
Iron regulated protein	06-Jun-2013	06-Jun-2013	Present	Present	Passed
Inactivation	08-May-2013	29-May-2013	No growth	No growth	Passed
Sterility	13-May-2013	28-May-2013	No growth	No growth	Passed
Formaldehyde	09-May-2013	09-May-2013	1.29 mg/ml	< 2 mg/ml	Passed
Antigen content	19-Jun-2013	19-Jun-2013	1.50 x 10 <sup>11</sup> *	n.a.	Passed
pH	14-May-2013	14-May-2013	6.6	6.3-7.2	Passed
Specific gravity	14-May-2013	14-May-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	08-Oct-2013	08-Oct-2013	52 ml	≥ 51 ml	Passed