

Manufacturer's Batch Protocol

Product: Bovipast RSP Vakcina A.U.V.

Batch: A084C01

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: **18 049**

Number of containers the release
is applied for: **18 049**

Number of doses per container: **10**

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

Date of expiry: **Mar-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**

09-Jan-2014/ce

1103027676/10

Manufacturer's Batch Protocol

Product: Bovipast RSP Vakcina A.U.V. Batch: A084C01

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:	A084C01
Batch number of final bulk:	A084
Pharmaceutical form of finished product:	Suspension for injection
Type of final container:	Hydrolytical class type I glass
Date of start of period of validity:	17-Sep-2013
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
20 JAN 2014


Manufacturer's Batch Protocol

Product: Bovipast RSP Vakcina A.U.V. Batch: A084C01

FINAL BATCH TESTING (FINISHED PRODUCT)

<u>Date on</u>	<u>Date off</u>	<u>Test results</u>
20-Sep-2013	11-Oct-2013	<u>Sterility (1.8)</u> Tested according to Ph. Eur. 0062/Ph.Eur.2.6.1 Result: No growth Threshold: No growth Conclusion: Passed
26-Jul-2013	16-Aug-2013	<u>Inactivation BRSV</u> Result: Inactivated Threshold: Inactivated Conclusion: Passed
26-Jul-2013	16-Aug-2013	<u>Inactivation PI3</u> Result: Inactivated Threshold: Inactivated Conclusion: Passed
03-Oct-2013	24-Oct-2013	<u>Inactivation M. haemolytica</u> Result: Inactivated Threshold: Inactivated Conclusion: Passed
17-Sep-2013	18-Oct-2013	<u>Potency using rabbits (1.6)</u> Result: Conform Threshold: Conform Conclusion: Passed
		<u>BRSV antibody</u> Single result: 10 / 25 / 54 / 85 / 46 / 42 / 104 / 139 / 70 / 256 Average: 83 Result standard: 12 Threshold: Antibody level not sign. lower than std. Conclusion: Passed
		<u>Identity BRSV</u> Result: Identity conform Threshold: Identity conform Conclusion: Passed

Manufacturer's Batch Protocol

Product: *Bovipast RSP Vakcina A.U.V.* Batch: *A084C01*

FINAL BATCH TESTING (FINISHED PRODUCT)

<u>Date on</u>	<u>Date off</u>	<u>Test results</u>
		<u>PI3 antibody</u>
		Single result: 90 / 50 / 160 / 80 / 80 / 120 / 80 / 120 / 160 / 160 Average: 110 Result standard: 47 Threshold: Antibody level not sign. lower than std. Conclusion: Passed
		<u>Identity PI3</u>
		Result: Identity conform Threshold: Identity conform Conclusion: Passed
		<u>M. haemolytica antibody</u>
		Single result: 50.26 / 52.80 / 45.81 / 48.57 / 34.13 / 57.41 / 52.65 / 40.09 / 55.41 / 62.61 % Average: 50 % Threshold: AB levels not sign. lower than passmark(37.1%) Conclusion: Passed
		<u>M. haemolytica quantification (1.9)</u>
		Single result: 0.302 / 0.337 / 0.373 / 0.458 / 0.293 / 0.311 Average: 0.346 1:5 diluted standard single result: 0.097 / 0.075 / 0.092 / 0.077 / 0.070 / 0.099 Average 1:5 diluted standard: 0.085 Threshold: O.D. significantly > 1:5 diluted std. Conclusion: Passed
11-Oct-2013	11-Oct-2013	<u>Aluminium (1.1)</u> Tested according to Ph. Eur. 2.5.13 Result: 3 mg/mL Threshold: 2 – 3 mg/mL Conclusion: Passed
23-Sep-2013	23-Sep-2013	<u>Formaldehyde (1.2)</u> Result: 0.16 mg/mL Threshold: <= 0.50 mg/mL Conclusion: Passed

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-Sep-2013	16-Sep-2013	<u>Sodium timerfonate (1.3)</u> Result: 0.0092 mg/mL Threshold: 0.0085 – 0.0115 mg/mL Conclusion: Passed
04-Sep-2013	04-Sep-2013	<u>pH (1.4)</u> Tested according to Ph. Eur. 2.2.3 Result: 7.8 Threshold: 6.9 – 7.9 Conclusion: Passed
07-Oct-2013	07-Oct-2013	<u>Endotoxin (1.7)</u> Result: 4.0×10^4 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: **03-Feb-2005**

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 SBRS13002			
Seed:	04-Feb-2013	04-Feb-2013	2400 m ^l
Harvest:	12-Feb-2013	12-Feb-2013	771.00 kg
Inactivation:	12-Feb-2013	16-Feb-2013	778.20 kg
Batch SBRS13003			
Seed:	11-Feb-2013	11-Feb-2013	2560.00 m ^l
Harvest:	19-Feb-2013	19-Feb-2013	767.50 kg
Inactivation:	19-Feb-2013	23-Feb-2013	774.70 kg

PRODUCTION OF PI3 COMPONENT:

<u>Production step</u>	<u>Start</u>	<u>End</u>	<u>Volume</u>
Batch SPI313001			
Seed:	08-Jan-2013	08-Jan-2013	3139.50 m ^l
Harvest:	14-Jan-2013	14-Jan-2013	913.80 kg
Inactivation:	14-Jan-2013	15-Jan-2013	922.30 kg
Batch SPI313002			
Seed:	22-Jan-2013	22-Jan-2013	2794.90 m ^l
Harvest:	28-Jan-2013	28-Jan-2013	907.80 kg
Inactivation:	28-Jan-2013	29-Jan-2013	916.30 kg

PRODUCTION OF M. HAEMOLYTICA COMPONENT:

<u>Production step</u>	<u>Start</u>	<u>End</u>	<u>Volume</u>
Batch LMHB002301			
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

CREATION OF THE FINISHED PRODUCT

BLENDING OF FINAL BULK:

Batch number:	D077
Start date:	11-Jul-2013
End date:	11-Jul-2013
Total volume:	3000.00 kg

Manufacturer's Batch Protocol

Product: Bovipast RSP Vakcina A.U.V.

Batch: A084C01

COMPOSITION OF THE FINAL BULK

Components	Batch no.	Total units
BRSV	SBR13002, SBR13003	750.48 kg
Pi3	SPI313001, SPI313002	600.62 kg
M. haemolytica	LMHB002301	31.80 kg
Adjuvant	SAL13001 SMS1309604	764.88 kg
Excipient	BMGM306931, BMGM213721, BMGM116581, SMS13103, SMS1302305, SMS1304802	852.22 kg

FILLING

Batch number of final bulk: **A084**
Final batch number: **A084C**
Start date: **20-Aug-2013**
End date: **20-Aug-2013**
Filled containers: **18 049**
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 SBR13002					
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)	15-Feb-2013	01-Mar-2013	No growth	No growth	Passed
Antigen content (TCID50)	18-Feb-2013	28-Feb-2013	5.9*	>= 5.4*	Passed
Identity	18-Feb-2013	28-Feb-2013	Conform	Conform	Passed
Sterility (after inac)	20-Feb-2013	06-Mar-2013	No growth	No growth	Passed
Freedom from live virus	01-Mar-2013	22-Mar-2013	No CPE	No CPE	Passed
pH	18-Feb-2013	18-Feb-2013	7.6	7.2 - 8.2	Passed

* Log10/ml

Batch SBR13003

Cell controls:

Microscopic inspection	08-Feb-2013	22-Feb-2013	No CPE	No CPE	Passed
Haemadsorption	22-Feb-2013	22-Feb-2013	No haemads.	No haemads.	Passed
Passage in vero cells	26-Feb-2013	12-Mar-2013	No CPE	No CPE	Passed
Sterility (before inac)	22-Feb-2013	08-Mar-2013	No growth	No growth	Passed
Antigen content (TCID50)	25-Feb-2013	07-Mar-2013	5.7*	>= 5.4*	Passed
Identity	25-Feb-2013	07-Mar-2013	Conform	Conform	Passed
Sterility (after inac)	27-Feb-2013	13-Mar-2013	No growth	No growth	Passed
Freedom from live virus	01-Mar-2013	22-Mar-2013	No CPE	No CPE	Passed
pH	25-Feb-2013	25-Feb-2013	7.7	7.2 - 8.2	Passed

* Log10/ml

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Batch: A084C01

In process controls PI3 antigen:

<u>Test</u>	<u>Start</u>	<u>End</u>	<u>Result</u>	<u>Thresholds</u>	<u>Conclusion</u>
Batch SPI313001					
Cell controls:					
Microscopic inspection	04-Jan-2013	18-Jan-2013	No CPE	No CPE	Passed
Haemadsorption	18-Jan-2013	18-Jan-2013	No haemads.	No haemads.	Passed
Passage in vero cells	22-Jan-2013	05-Feb-2013	No CPE	No CPE	Passed
Sterility (before inac)	16-Jan-2013	30-Jan-2013	No growth	No growth	Passed
Antigen content (TCID50)	15-Jan-2013	25-Jan-2013	7.6*	>= 7.3*	Passed
Identity	15-Jan-2013	25-Jan-2013	Conform	Conform	Passed
Sterility (after inac)	17-Jan-2013	31-Jan-2013	No growth	No growth	Passed
Freedom from live virus	18-Jan-2013	08-Feb-2013	No CPE	No CPE	Passed
pH	15-Jan-2013	15-Jan-2013	7.7	7.2 - 8.2	Passed
* Log10/ml					

Batch SPI313002

Cell controls:

Microscopic inspection	18-Jan-2013	01-Feb-2013	No CPE	No CPE	Passed
Haemadsorption	01-Feb-2013	01-Feb-2013	No haemads.	No haemads.	Passed
Passage in vero cells	05-Feb-2013	19-Feb-2013	No CPE	No CPE	Passed
Sterility (before inac)	30-Jan-2013	13-Feb-2013	No growth	No growth	Passed
Antigen content (TCID50)	12-Feb-2013	22-Feb-2013	7.9*	>= 7.3*	Passed
Identity	12-Feb-2013	22-Feb-2013	Conform	Conform	Passed
Sterility (after inac)	31-Jan-2013	14-Feb-2013	No growth	No growth	Passed
Freedom from live virus	01-Feb-2013	01-Mar-2013	No CPE	No CPE	Passed
pH	29-Jan-2013	29-Jan-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 LMHB002301					
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	1.3 mg/ml	< 2 mg/ml	Passed
Antigen content	19-Mar-2013	19-Mar-2013	1.88 10 ¹¹ *	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	1038	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	20-Aug-2013	20-Aug-2013	52 ml	≥ 51 ml	Passed