

Product Quality and Disposition Department

Diphtheria, tetanus, pertussis (acellular, component),
 hepatitis B (rDNA), poliomyelitis (inactivated) and Haemophilus
 influenzae type b conjugate vaccine (adsorbed) lot n° S4313 (clinical batch) 171/180

Polysaccharide content :



Method	: High Performance Anion Exchange Chromatography with Pulsed Amperometric Detection method (HPAEC-PAD)
Standard	: CP09E055
Date	: 10.12.2009
Non adsorbed PRP	: 10 µg/dose
Depolymerized PRP	: 3.7 % - Conforms

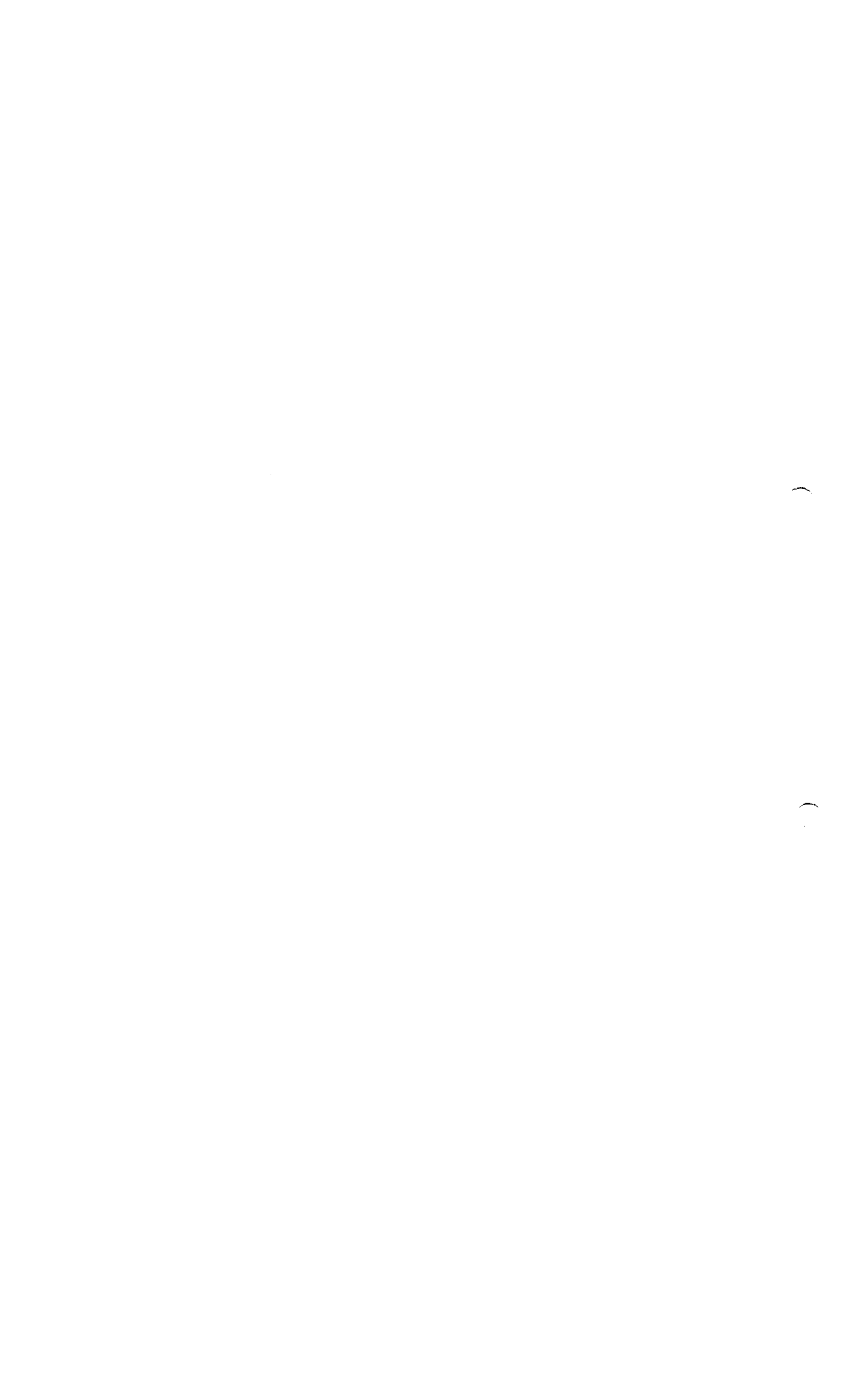
Percent adsorption – Diphtheria toxoid:

Method	: Rocket Immunoelectrophoresis method
Date	: 01.12.2009
Result	: 54 %

Percent adsorption – Hepatitis B:

Method	: ELISA
Date	: 27.11.2009
Result	: 97 %

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Diphtheria potency

Method : European Pharmacopoeia
 Strain and sex of animals : Guinea pigs - Dunkin-Hartley - female
 Weight : 250 - 350 g
 Number of animals per dose : 8

Immunization


Date : 23.11.2009
 Volume tested : 1 ml
 Route : Subcutaneous

Challenge


Date : 21.12.2009
 Challenge dose : 0.0512 - 0.0128 - 0.0032 - 0.0008
 0.0002 and 0.00005 Lf/0.2 ml
 Route : Intradermal
 Reading date : 23.12.2009

Results	Dilutions	Score	Log ED ₅₀
Reference toxoid BRP - D4 97 IU/ml	1/16	28/42	- 1.541
	1/32	26/48	
	1/64	19/48	
	1/128	9/48	
Product tested FDV01416	1/17.5	30/48	- 1.613
	1/35	27/48	
	1/70	22/48	
	1/140	10/48	

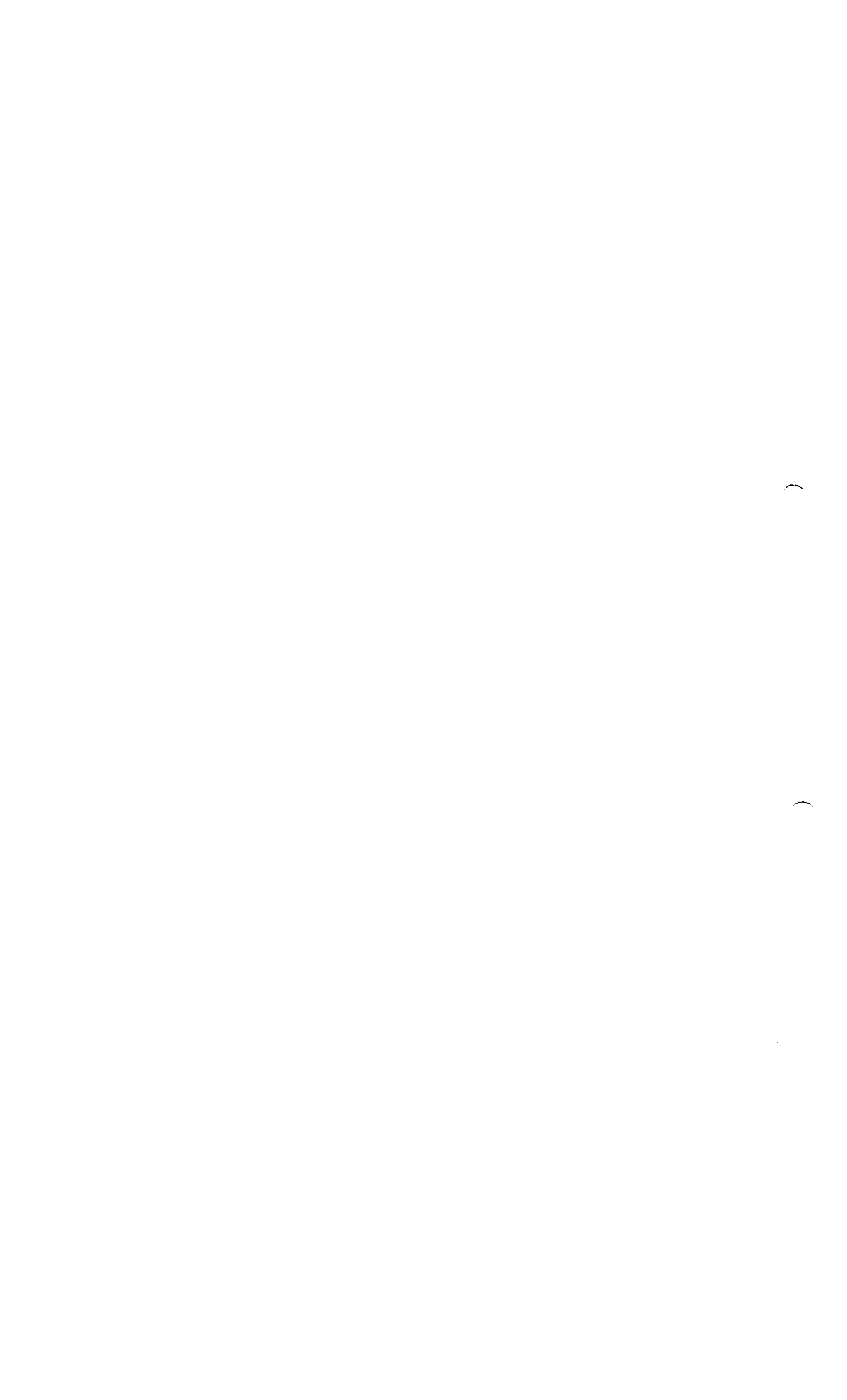
Potency : 57 IU/dose
 Confidence limits (P=0.95) : 43 - 82 IU/dose



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Tetanus potency

Method : European Pharmacopoeia
 Strain and sex of animals : Mice Swiss OF1 - Female
 Age : 5 weeks
 Number of animals per dose : 16

Immunization



Date : 03.12.2009
 Volume : 0.5 ml
 Route : Subcutaneous

Challenge

Date : 31.12.2009
 Challenge dose : 1/320
 Volume : 0.5 ml
 Route : Subcutaneous
 Reading date : 04.01.2010

Results	Dilutions	Score/Total	Log ED ₅₀
Reference toxoid NIBSC-T 98/552 250 IU/ml	1/25	16/16	- 1.948
	1/50	14/16	
	1/100	8/16	
	1/200	0/16	
Product tested FDV01416	1/150	10/16	- 2.617
	1/300	9/16	
	1/600	6/16	
	1/1200	0/16	

Potency : 584 IU/dose
 Confidence limits (P=0.95) : 413 – 795 IU/dose


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Immunogenicity Pertussis in mice

Animals and sex : Mice Swiss OF1- Female
Weight : 20 - 22 g
Number of animals per group : 10

Immunization

Date : 26.11.2009
Volume : 0.5 ml
Route : Intraperitoneal
Reference vaccine : PFAGI003-03
Dose per mouse : 1/5 human dose

Bleeding date : 24.12.2009

Titration

1. Anti-PT titers

Method : ELISA
Pertussis toxin for coating : FA287985
Standard anti-PT serum : BRP BATCH1
Date : 07.01.2010
Results
Reference vaccine : 201 EU/ml (163 - 248)
Product tested : 180 EU/ml (104 - 311)
Probability : >0.50 (p >0.05)

2. Anti-FHA titers

Method : ELISA
FHA for coating : FA088651
Standard anti-FHA serum : BRP BATCH1
Date : 06.01.2010
Results
Reference vaccine : 130 EU/ml (82 - 208)
Product tested : 147 EU/ml (96 - 225)
Probability : >0.50 (p >0.05)

Conclusion : Conforms

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D Antigen content


Method : ELISA
Standard : 11.07.07 versus EWS
Date : 16.02.2010


	D Antigen unit/dose		
	Type 1	Type 2	Type 3
Product tested	29	6	26

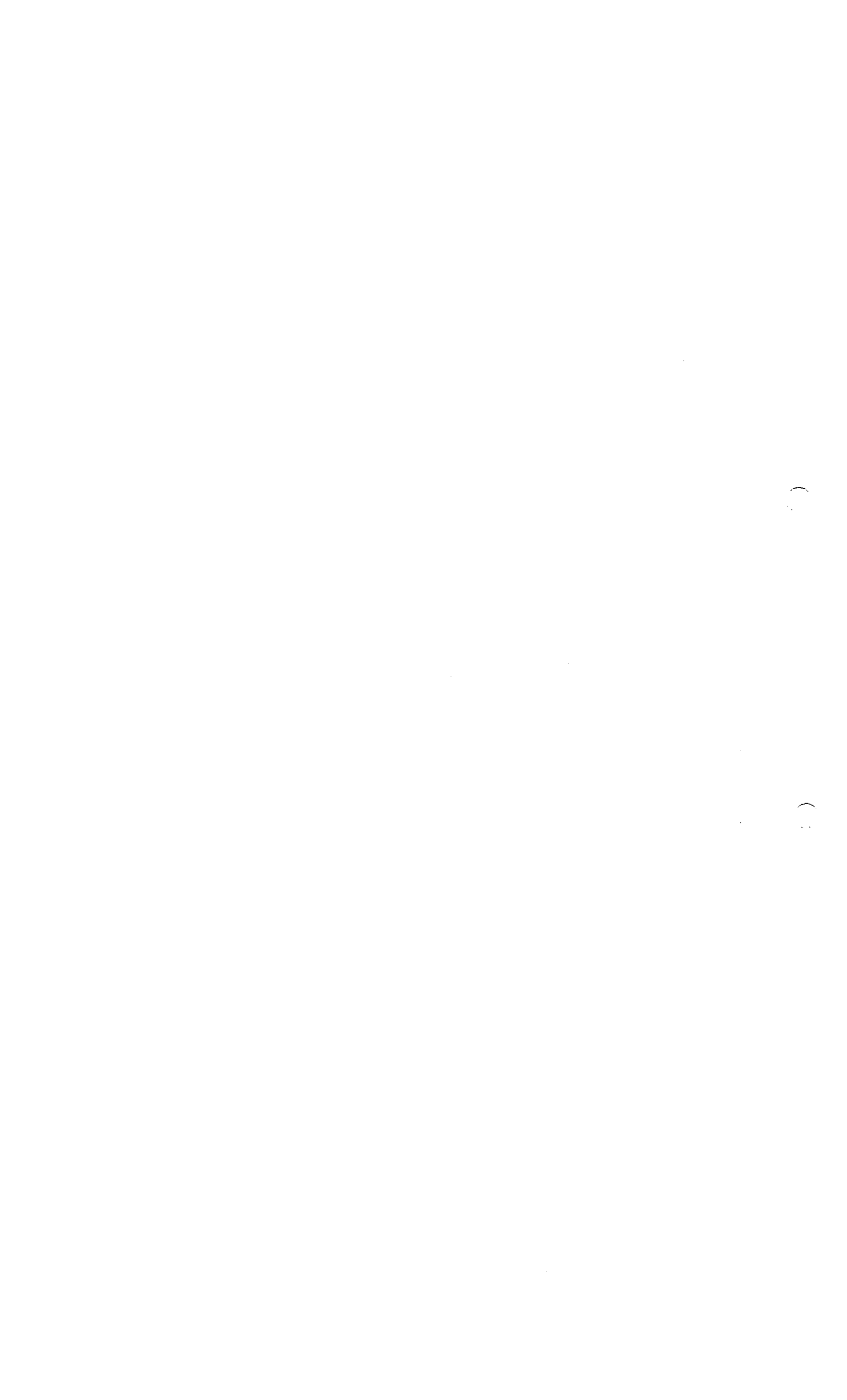
Result : Conforms

Hepatitis B in vitro Relative Potency

Method : ELISA
Date : 27.11.2009
Result : Conforms


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PART 3
FINAL PRODUCT


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FINAL PRODUCT

TESTS	SPECIFICATIONS
APPEARANCE	Whitish and cloudy suspension
pH	6.5 - 7.5
EXTRACTABLE VOLUME	At least the nominal volume
ALUMINIUM CONTENT	0.40 - 0.80 mg/dose
BACTERIAL AND FUNGAL STERILITY	No microbial growth
PYROGEN TEST	Conforms to Ph. Eur. criterion
ABNORMAL TOXICITY TEST	No death nor sickness sign At time of release, the test was performed
IDENTITY OF EACH VALENCE : DIPHTHERIA, TETANUS, PERTUSSIS, POLIOMYELITIS, HEPATITIS B, HAEMOPHILUS	Positive


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FINAL PRODUCT
Lot number : S4313

Date of manufacture: 09.02.2010

CONTROLS :

Appearance

Method : Visual inspection
Date : 04.03.2010
Result : Conforms

pH

Method : Glass electrode
Date : 08.03.2010
Result : 7.18 - Conforms

Extractable Volume

Method : European Pharmacopoeia
Date : 08.03.2010
Result : Conforms

Aluminium content

Method : Complexometry
Date : 08.03.2010
Result : 0.60 mg/dose - Conforms

Bacterial and fungal sterility

Method : Membrane filtration
Media : Thioglycollate medium | Soybean-Casein Digest medium
Temperature : 30-35° C | 20-25° C
Number of units tested : 40
Inoculum per Steritest : 10 ml | 10 ml
Volume of medium per Steritest : 100 ml | 100 ml
Test on : 17.02.2010
Test off : 03.03.2010
Result : No microbial growth - Conforms

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Pyrogen test

Method : by intravenous injection 0.1 µg/ml/kg of the
rabbit body weight
Date : 11.03.2010
Number of rabbits : 3

Weight of each rabbits (kg)	Initial temperature in °C (A)	Intravenous dose (ml)	Maximum temperature in °C (B)	Response (B) - (A)
2.5	39.07	0.5	39.21	0.14
2.6	38.89	0.5	39.29	0.40
2.3	39.48	0.5	39.57	0.09

The sum of the 3 individual maximum temperature rises : 0.63 °C

Result : **Conforms**

Diphtheria, Tetanus, Pertussis (FHA and Pertussis toxoid), Poliomyelitis, Hepatitis B and Haemophilus identity

Method : Luminex
Date : 14.04.2010 and 15.04.2010
Result : **Positive - Conforms**

Abnormal toxicity

Animals	:	Mice		Guinea pigs
Number of animals	:	5		2
Volume injected	:	0.5 ml		5 ml
Route of injection	:	Intraperitoneal		
Test on	:	03.03.10		
Test off	:	10.03.10		
Result	:	No death nor sickness sign - Conforms		





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**DIPHTHERIA, TETANUS, PERTUSSIS (ACELLULAR,
COMPONENT), HEPATITIS B (RDNA), POLIOMYELITIS
(INACTIVATED) AND HAEMOPHILUS INFLUENZAE TYPE B
CONJUGATE VACCINE (ADSORBED)**

Lot number **S4314**

Clinical Batch


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SUMMARY PROTOCOL FOR DIPHTHERIA, TETANUS, PERTUSSIS (ACELLULAR, COMPONENT), HEPATITIS B (RDNA), POLIOMYELITIS (INACTIVATED) AND HAEMOPHILUS INFLUENZAE TYPE B CONJUGATE VACCINE (ADSORBED)

Name and address of manufacturer	Sanofi Pasteur S.A. 2 avenue Pont Pasteur 69007 Lyon
Sites of production	Sanofi Pasteur S.A. 1541, avenue Marcel Merieux 69280 Marcy l'Etoile Parc Industriel d'Incarville 27101 Val de Reuil Cedex
Clinical batch submitted according to the procedure number (Article 58)	: EMEA/H/W/002495
Lot number	: S4314
Date of manufacture of final lot	: 10.02.2010
Final bulk	: FDV01420
Volume of final bulk	: 242.8 Liters
Nature of final product	: suspension for injection
Type of container	: white glass (type I) vial
Number of doses per container	: 1 per vial
Number of containers	: 19 765
Target group	: immunizing agent
Volume of single dose	: 0.5 ml
Release date	: 22.07.2010
Starting of validity period	: 07.12.2009
Expiry date	: November 2012
Storage temperature	: + 5 °C ± 3°C

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