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The vaccines division of sanofi-aventis Group

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° S4312 (clinical batch) 227/229

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FINAL PRODUCT

Lot number : S4312

Date of manufacture: **08.02.2010**

CONTROLS :

Appearance

Method	: Visual inspection
Date	: **25.02.2010**
Result	: **Conforms**

pH

Method	: Glass electrode
Date	: **01.03.2010**
Result	: **7.29 - Conforms**

Extractable Volume

Method	: European Pharmacopoeia
Date	: **01.03.2010**
Result	: **Conforms**

Aluminium content

Method	: Complexometry
Date	: **02.03.2010**
Result	: **0.62** 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	**39.17**	**0.5**	**39.30**	**0.13**
2.3	**38.81**	**0.5**	**38.94**	**0.13**
2.4	**38.92**	**0.5**	**39.02**	**0.10**

The sum of the 3 individual maximum temperature rises : **0.36** °C
Result : **Conforms**

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

Method : Luminex
Date : **08.04.2010 and 09.04.2010**
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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MANUFACTURER' S CERTIFICATION

I herewith certify that **DIPHTHERIA, TETANUS, PERTUSSIS (ACELLULAR, COMPONENT), HEPATITIS B (RDNA), POLIOMYELITIS (INACTIVATED) AND HAEMOPHILUS INFLUENZAE TYPE B CONJUGATE VACCINE (ADSORBED)**, batch number **S4312**, was manufactured and tested according to cGMP and was submitted in the frame of the CTD submission via the Article 58 of regulation N°726/2004 in july 2011, procedure number : EMEA/H/W/002495.
This includes that, for any materials derived from ruminants (bovine, ovine, caprine) used in the manufacture and/or formulation of the batch of product specified above, all measures have been taken to demonstrate compliance with Directive 2001/83/EC and amending directives 2003/63/EC and 2004/27/EC .

GENERAL CONCLUSION : Conforms

Date : 07 December 2011

Name : A PADIEU - SEQUEIRA

R&D QA **Product Quality and Disposition Department**

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A.N.M.A.T. FOLIO 382 MESA DE ENTRADAS

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

Lot number **S4313**

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	: **S4313**
Date of manufacture of final lot	: **09.02.2010**
Final bulk	: **FDV01416**
Volume of final bulk	: **240.8** 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	: **20 170**
Target group	: immunizing agent
Volume of single dose	: 0.5 ml
Release date	: **22.07.2010**
Starting of validity period	: **23.11.2009**
Expiry date	: **October 2012**
Storage temperature	: + 5 °C ± 3°C

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Diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA),poliomyelitis (inactivated) and Haemophilus influenzae type b conjugate vaccine (adsorbed) lot n° S4313 (clinical batch) 3/180

Composition of single human dose * :

Purified diphtheria toxoid	: 30 Lf (≥ 20 IU +)
Purified tetanus toxoid	: 10 Lf (≥ 40 IU +)
Bordetella pertussis antigens	
Adsorbed purified pertussis toxoid	: 25 µg
Adsorbed purified filamentous haemagglutinin	: 25 µg
Inactived poliomyelitis virus (produced on Vero cells)	
Type 1 (Mahoney)	: 40 DU §
Type 2 (MEF-1)	: 8 DU §
Type 3 (Saukett)	: 32 DU §
Hepatitis B surface antigen **	: 10 µg
Haemophilus influenzae type b polysaccharide (polyribosylribitol phosphate)	: 12 µg
Conjugated to Tetanus protein (PRP-T)	: 18-30 µg
Aluminium hydroxide, hydrated, for adsorption	: 0.6 mg Al^{3+}
Buffer solution :	
Disodium hydrogen phosphate	: 1.528 mg
Potassium dihydrogen phosphate	: 1.552 mg
Essential amino acids ∓	: 1.115 mg
Trometamol	: 0.1515 mg
Saccharose	: 10.625 mg
Water for injections	: up to 0.5 ml

* NaOH, acetic acid, or HCl can be used for pH adjustment.these components are only present in trace amount.

+ As lower confidence limit (p = 0.95)

§ Or equivalent antigenic quantity determined by suitable immunochemichal method

** Produced in yeast *Hansenula polymorpha* cells by recombinant DNA technology

∓ Essentials amino acids including L-phenylalanine

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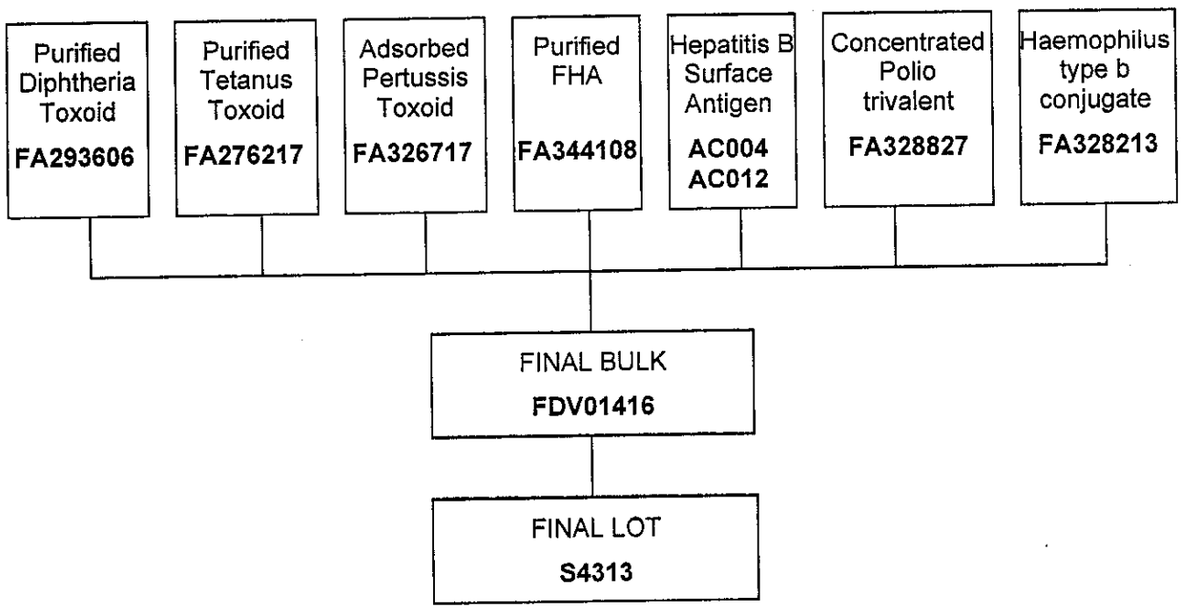
PRODUCTION FLOW SHEET



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PART 1

ACTIVE INGREDIENTS

A - PURIFIED DIPHTHERIA TOXOID

B - PURIFIED TETANUS TOXOID

C - 2 COMPONENT ACELLULAR PERTUSSIS

D - HEPATITIS B

E - INACTIVATED POLIOMYELITIS TRIVALENT

F - HAEMOPHILUS type b CONJUGATE

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- A - PURIFIED DIPHTHERIA TOXOID

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