

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) 173/180

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

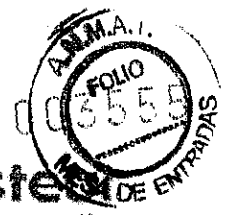
Date : 31.12.2009
 Challenge dose : 1/320
 Volume : 0.5 ml
 Route : Subcutaneous
 Reading date : 04.01.2010

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


 ROXANA MONTEMILONE
 DIRECTORA TÉCNICA
 SANOFI PASTEUR S.A.


 CHRISTIAN DOMINGUEZ
 MODERADOR
 SANOFI PASTEUR S.A.



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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

ROXANA MONTEMILONE
DIRECTORA TÉCNICA
SANOFI PASTEUR S.A.

CHRISTIAN DOMINGUEZ
MODERADO
SANOFI PASTEUR S.A.





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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


 ROXANA MONTEMILONE
 DIRECTORA TÉCNICA
 SANOFI PASTEUR S.A.


 CHRISTIAN DOMÍNGUEZ
 GERENTE
 SANOFI PASTEUR S.A.





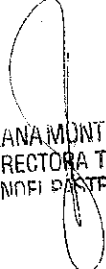
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PART 3
FINAL PRODUCT


ROXANA MONTEMILONE
DIRECTORA TÉCNICA
SANOFI PASTEUR S.A.


CHRISTIAN DOMINGUEZ
AUTORIZADO
SANOFI PASTEUR S.A.





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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


 ROXANA MONTEMILONE
 DIRECTORA TÉCNICA
 SANOFI PASTEUR S.A.


 CHRISTIAN DOMINGUEZ
 SUPERGRADO
 SANOFI PASTEUR S.A.





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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

ROXANA MONTEMILONE
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 SANOFI PASTEUR S.A.

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 APCDERADO
 SANOFI PASTEUR S.A.





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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		

ROXANA MONTEMILONE
 DIRECTORA TÉCNICA
 SANOFI PASTEUR S.A.

CHRISTIAN DOMÍNGUEZ
 AYUDERADO
 SANOFI PASTEUR S.A.



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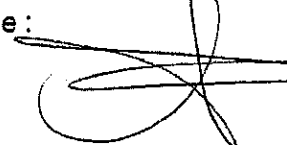
MANUFACTURER' S CERTIFICATION

I herewith certify that **DIPHTHERIA, TETANUS, PERTUSSIS (ACELLULAR, COMPONENT), HEPATITIS B (RDNA), POLIOMYELITIS (INACTIVATED) AND HAEMOPHILUS INFLUENZAE TYPE B CONJUGATE VACCINE (ADSORBED)**, batch number **S4313**, 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. PASTIEU-BEQUERIA

RASAA Product Quality and Disposition Department


ROXANA MONTEMILONE
DIRECTORA TÉCNICA
SANOFI PASTEUR S.A.


CHRISTIAN DOMINGUEZ
APODERADO
SANOFI PASTEUR S.A.

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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


ROXANA MONTEMILONE
DIRECTORA TÉCNICA
SANOFI PASTEUR S.A.


CHRISTIAN DOMINGUEZ
MODERADO
SANOFI PASTEUR S.A.




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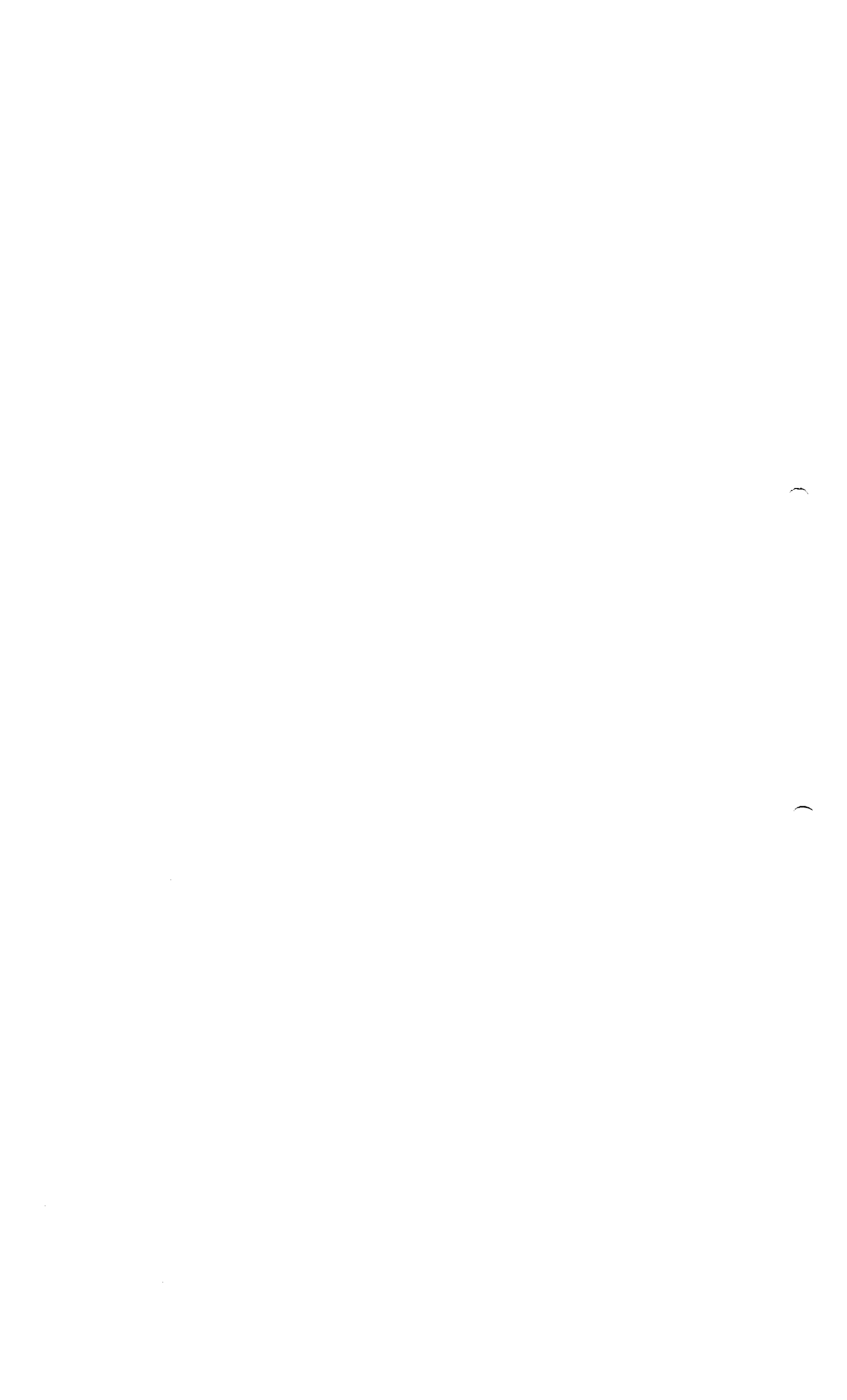
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Clinical Batch


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DIRECTORA TÉCNICA
SANOFI PASTEUR S.A.


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SANOFI PASTEUR S.A.



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 influenzae type b conjugate vaccine (adsorbed) lot n° S4314 (clinical batch)** 2/211

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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


ROXANA MONTEMILONE
 DIRECTORA TÉCNICA
 SANOFI PASTEUR S.A.

CHRISTIAN DOMINGUEZ
 SUPERADJUNTO
 SANOFI PASTEUR S.A.



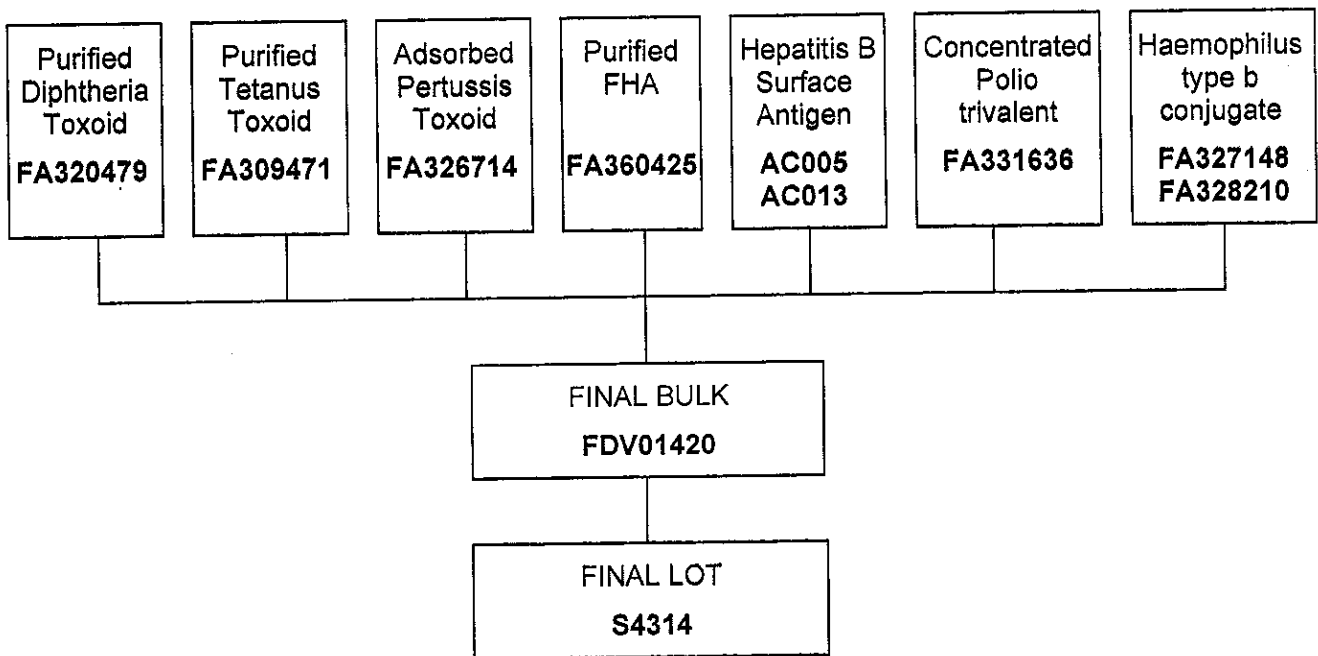
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PRODUCTION FLOW SHEET




 ROXANA MONTEMILONE
 DIRECTORA TÉCNICA
 SANOFI PASTEUR S.A.


 CHRISTIAN DOMÍNGUEZ
 COORDINADOR
 SANOFI PASTEUR S.A.



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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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ROXANA MONTEMILONE
DIRECTORA TÉCNICA
SANOFI PASTEUR S.A.


CHRISTIAN DOMINGUEZ
SUPERVISOR
SANOFI PASTEUR S.A.

