

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)

34/180

**NATIVE PURIFIED PERTUSSIS TOXIN**

Lot number : FA297798

Date of manufacture : 18.02.2008  
 Storage temperature : + 5°C ± 3°C  
 Expiry date : 18 FEBRUARY 2012  
 Volume : 13.361 liters

**CONTROLS :**

**Protein content**

Method : Spectrophotometry  
 Date : 21.02.08  
 Result : 1259.40 µg/ml

**SDS-page**

Method : Polyacrylamide Gel Electrophoresis  
 Date : 13.03.08  
 Result : Electrophoresis profile comparable to the profile of  
 the reference (5 bands between 30 and 14 kDa) -  
 Conforms.

**Pertussis toxin identification**


Method : Double Diffusion in Gel  
 Date : 26.02.08  
 Result : Positive - Conforms


**Clustering activity on Chinese Hamster Ovary cells**

Method : Clusters Assay on CHO Cells  
 Date : 27.02.08

	CPU/µg
Reference 90/518	89600
Product	153600

Result : Conforms

  
 RUXANA MONTEMILONE  
 DIRECTORA TÉCNICA  
 SANOFI PASTEUR S.A.

  
 CHRISTIAN DOMINGUEZ  
 SUPERVISOR  
 SANOFI PASTEUR S.A.





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influenzae type b conjugate vaccine (adsorbed) lot n° S4313 (clinical batch) 35/180  
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**Haemagglutining activity**

Method	: Haemagglutination of goose red blood cells by PT
Date	: 06.03.08
Result	: 102449 HAU/mg IHA with cholesterol : 0 % - Conforms

  
ROXANA MONTEMILONE  
DIRECTORA TÉCNICA  
SANOFI PASTEUR S.A.

  
CHRISTIAN DOMINGUEZ  
GERENTE  
SANOFI PASTEUR S.A.





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The vaccines division of sanofi-aventis Group

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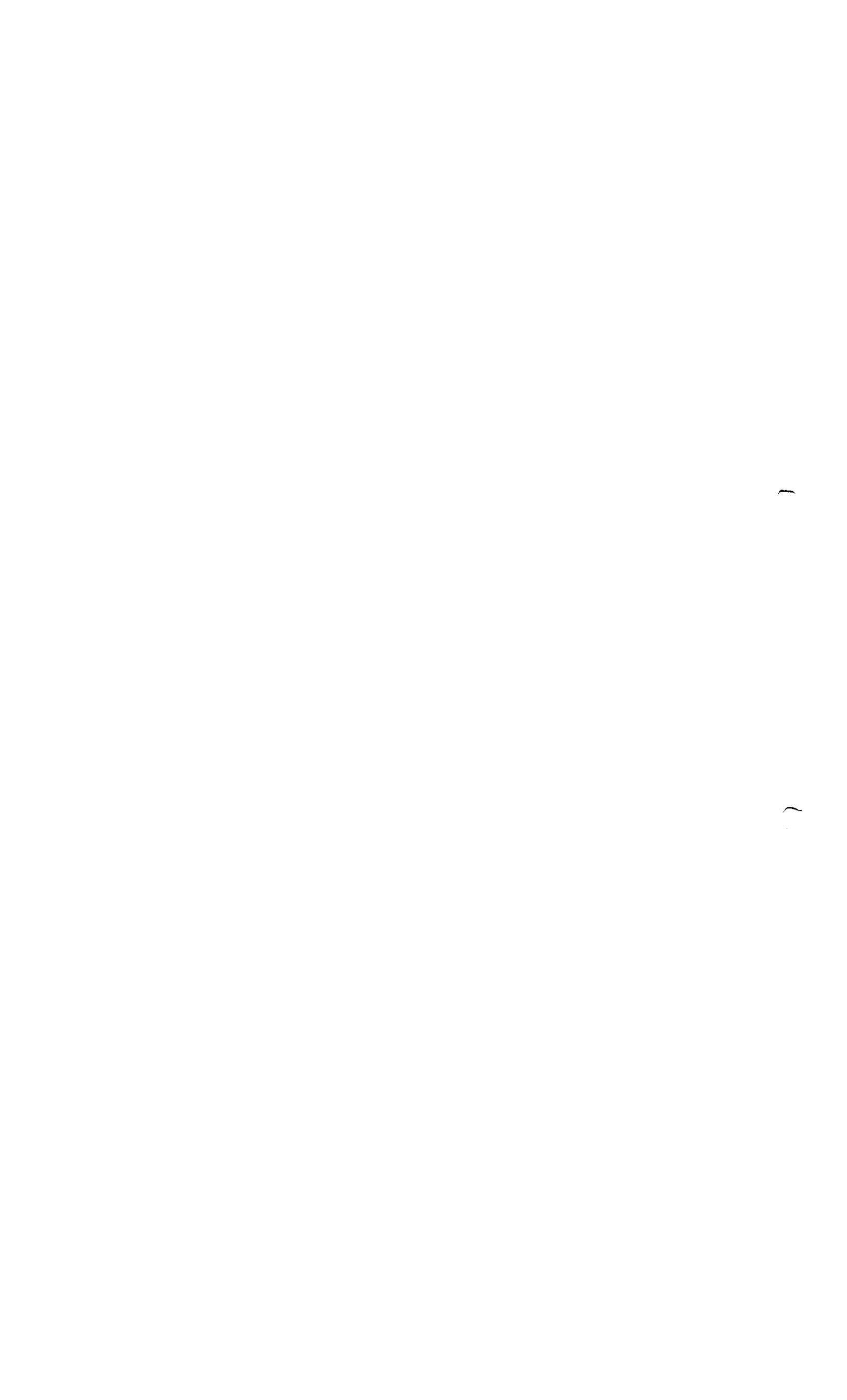
**ADSORBED PURIFIED PERTUSSIS TOXOID**

TESTS	SPECIFICATIONS
<b>PURIFIED PERTUSSIS TOXOID IN SOLUTION</b>	
PROTEIN CONTENT	50 – 180 µg/ml
BACTERIAL ENDOTOXINS	≤ 3 500 UI/mg protein
RESIDUAL GLUTARALDEHYDE CONTENT	< 8 µg/ml
ANTIGENICITY	Specific activity (EU/mg of protein) ≥ lower confidence limit (p = 0.95) of the specific activity of SP batches
CLUSTERING ACTIVITY ON CHO CELLS	No cytopathic effect
IRREVERSIBILITY OF PERTUSSIS TOXOID	≥ 95% of survival
<b>ADSORBED PURIFIED PERTUSSIS TOXOID</b>	
ALUMINIUM CONTENT	0.6 - 1.4 mg Al/mg of protein
pH	6.2 - 8.2
PERTUSSIS IDENTIFICATION	Positive
BACTERIAL AND FUNGAL STERILITY	No microbial growth

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 ROXANA MONTEMILONE  
 DIRECTORA TÉCNICA  
 SANOFI PASTEUR S.A.

  
 CHRISTIAN DOMÍNGUEZ  
 GERENTE  
 SANOFI PASTEUR S.A.



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 influenzae type b conjugate vaccine (adsorbed) lot n° S4313 (clinical batch) 37/180

**ADSORBED PURIFIED PERTUSSIS TOXOID**  
 Lot number : FA326717

Date of manufacture : 31.10.2008  
 Storage temperature : + 5°C ± 3°C  
 Expiry date : 31 OCTOBER 2012  
 Volume : 33.000 liters

**PURIFIED PERTUSSIS TOXOID IN SOLUTION :**

**CONTROLS :**

**Protein content**

Method : Spectrophotometry  
 Date : 29.10.08  
 Result : 122.22 µg/ml - Conforms

**Bacterial endotoxins**

Method : LAL  
 Date : 04.11.08  
 Result : <4.09 IU/mg of protein

**Residual glutaraldehyde content**



Method : Spectrophotometry  
 Date : 02.12.08  
 Result : <2 µg/ml – Conforms

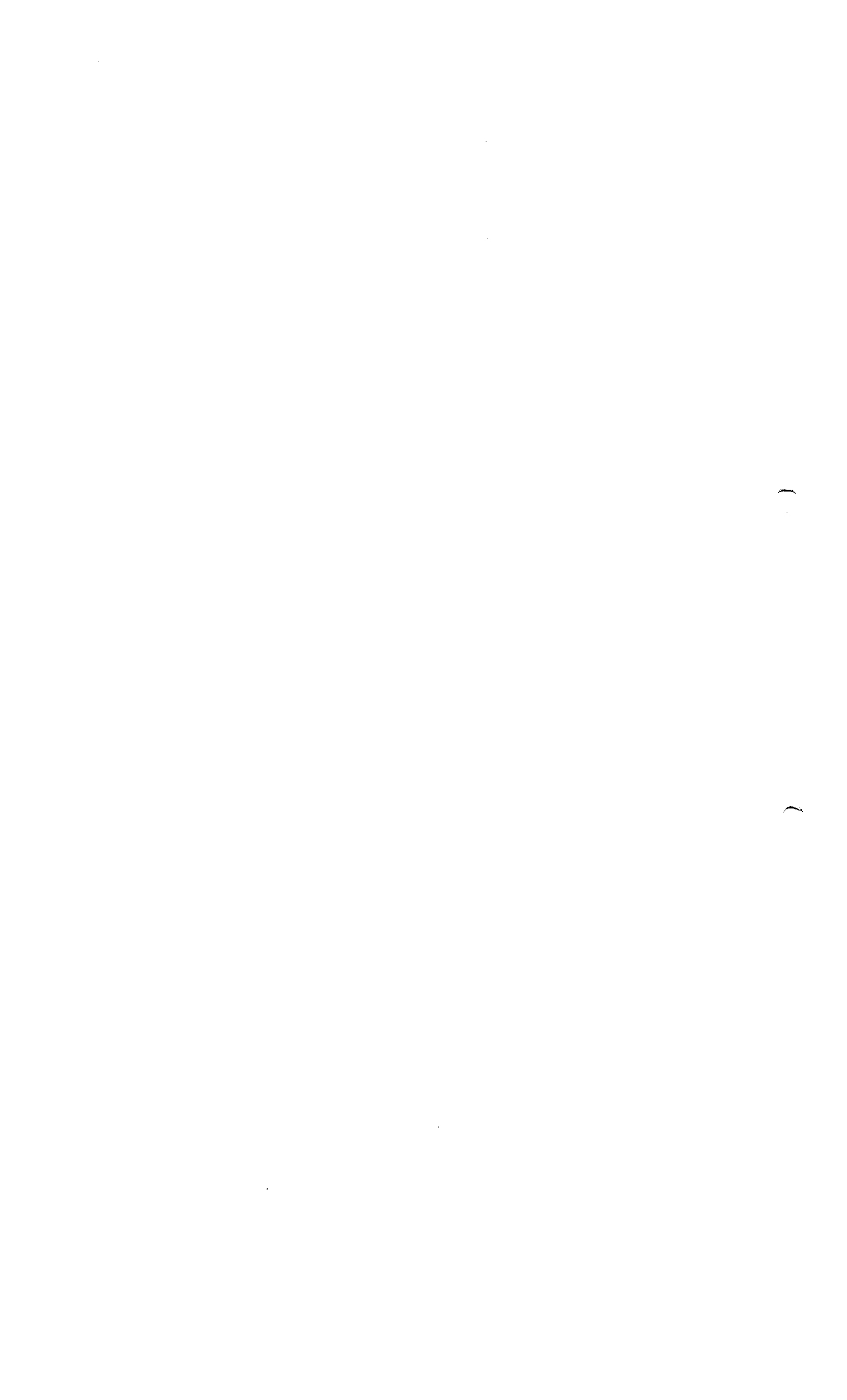
**Antigenicity**

Method : ELISA  
 Date : 19.11.08

	EU/mg of protein
Lower confidence limit (P=0.95) of the specific activity of SP batches	<b>24.5</b>
Product	<b>79.1</b>

Result : Conforms

  
 ROXANA MONTEMILONE  
 DIRECTORA TÉCNICA  
 SANOFI PASTEUR S.A.  
  
 CHRISTIAN DOMINGUEZ  
 GERENTE  
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 influenzae type b conjugate vaccine (adsorbed) lot n° S4313 (clinical batch) 38/180  
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**Clustering activity on Chinese Hamster Ovary cells**

Method : Clusters Assay on CHO Cells  
 Date : 07.01.09  
 Result : No cytopathic effect

**Irreversibility of pertussis toxoid**

Injection (Day 0)

Animals and sex : mice CD1 - Female  
 Route : Intraperitoneal  
 Dose tested per mouse : 2 human doses (1ml)  
 Date of injection : 22.01.09

Histamine challenge (Day 5)

Challenge dose per mouse : 2 mg histamine base  
 Route : Intraperitoneal  
 Date of injection : 27.01.09

Reading date (Day 6) : 28.01.09  
 Result (+5°C and +37°C) : ≥ 95% of survival - Conforms

**ADSORBED PURIFIED PERTUSSIS TOXOID :**

**CONTROLS :**

**Aluminium content**



Method : Complexometry  
 Date : 17.11.08  
 Result : 0.98 mgAl/mg of protein - Conforms

**pH**

Method : Glass electrode  
 Date : 06.11.08  
 Result : 6.48 - Conforms

**Pertussis Identification**

Method : Double diffusion in Gel  
 Date : 06.11.08  
 Result : Positive - Conforms

  
 ROXANA MONTEMILONE  
 DIRECTORA TÉCNICA  
 SANOFI PASTEUR S.A.  
  
 CHRISTIAN DOMINGUEZ  
 GERENTE  
 SANOFI PASTEUR S.A.



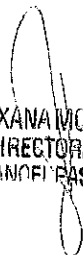

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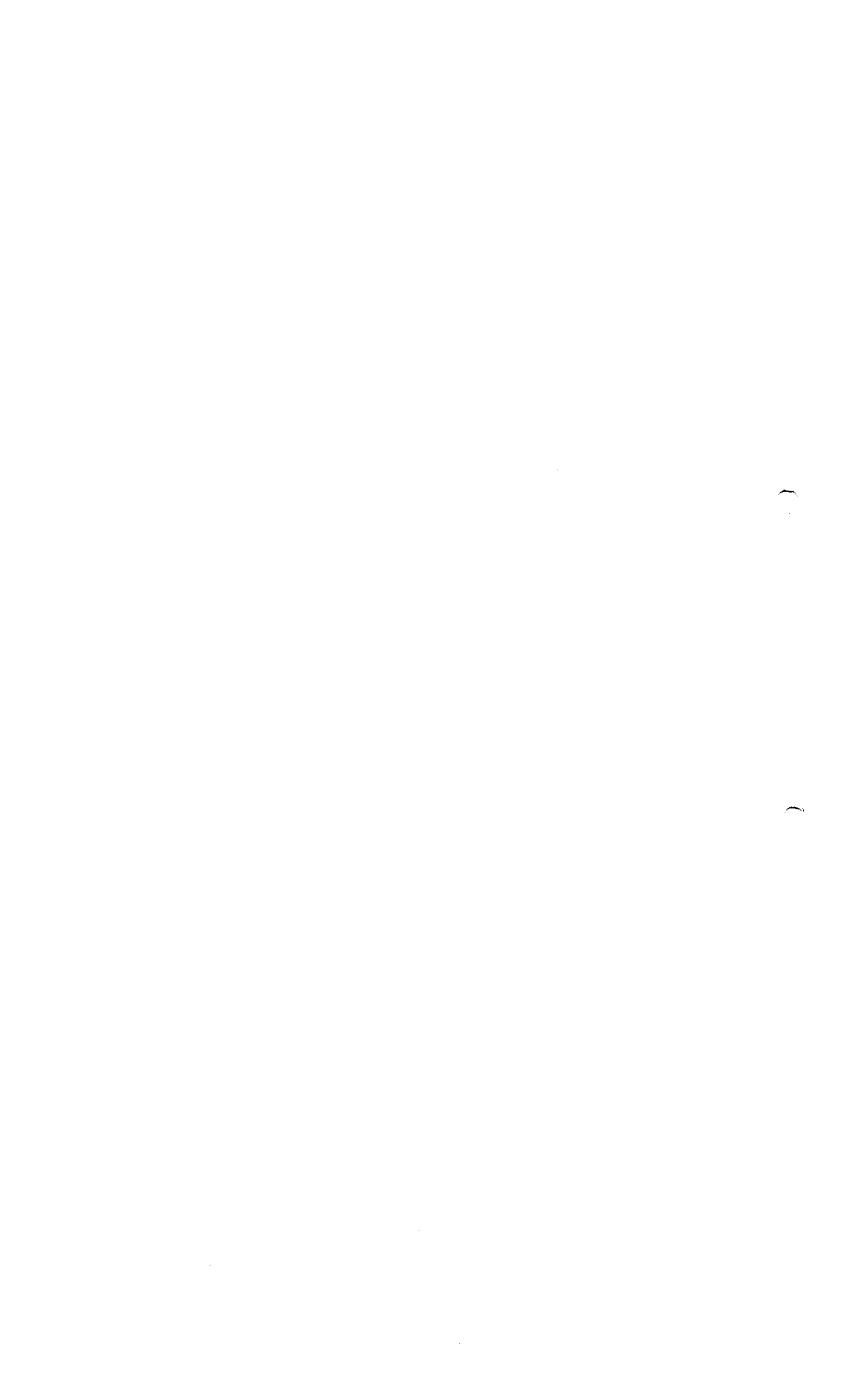
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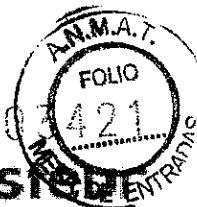
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**Bacterial and fungal sterility**

Method	:	Membrane filtration	
Media	:	Thioglycollate medium	Soybean Casein Digest medium
Temperatures	:	30-35° C	20-25° C
Volume tested	:	20 ml	
Inoculum per Steritest	:	10 ml	10 ml
Volume of medium per Steritest	:	100 ml	100 ml
Test on	:	04.11.08	
Test off	:	18.11.08	
Result	:	No microbial growth - Conforms	


  
 ROXANA MONTEMILONE      CHRISTIAN DOMINGUEZ  
 DIRECTORA TÉCNICA      SUPERADO  
 SANOFI PASTEUR S.A.      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 n° S4313 (clinical batch)


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NATIVE PURIFIED FHA

TESTS	SPECIFICATIONS
PROTEIN CONTENT	For calculation
SDS-PAGE	Electrophoresis profile comparable to the profile of the reference (one major band at about 220 kDa $\geq$ 70 % of total and some minor bands)
FHA IDENTIFICATION	Positive
CLUSTERING ACTIVITY ON CHO CELLS	No cytopathic effect
HAEMAGGLUTININATING ACTIVITY	200 000 – 2 500 000 HAU/mg of protein IHA with cholesterol : $\geq$ 80 %

  
 ROXANA MONTEMILONE  
 DIRECTORA TÉCNICA  
 SANOFI PASTEUR S.A.

  
 CHRISTIAN DOMÍNGUEZ  
 GERENTE  
 SANOFI PASTEUR S.A.



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 influenzae type b conjugate vaccine (adsorbed) lot n° S4313 (clinical batch)

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**NATIVE PURIFIED FHA**

**Lot number : FA317471**

Date of manufacture : **31.07.2008**  
 Storage temperature : **+ 5°C ± 3°C**  
 Expiry date : **31 JULY 2012**  
 Volume : **57.100 liters**

**CONTROLS :**

**Protein content**

Method : Spectrophotometry  
 Date : **09.09.08**  
 Result : **1240.95 mg/ml**

**SDS-page**

Method : Polyacrylamide Gel Electrophoresis  
 Date : **24.09.08**  
 Result : **Electrophoresis profile comparable to the profile of the reference (one major band at about 220 kDa ≥ 70 % of total and some minor bands) - Conforms**

**FHA identification**

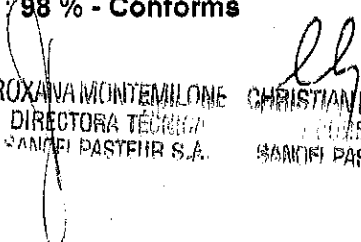
Method : Double Diffusion in Gel  
 Date : **25.09.08**  
 Result : **Positive - Conforms**

**Clustering activity on Chinese Hamster Ovary cells**

Method : Clusters Assay on CHO Cells  
 Date : **24.09.08**  
 Result : **No cytopathic effect**

**Haemagglutinating activity**

Method : Haemagglutination of goose red blood cells by PT  
 Date : **23.09.08**  
 Result : **2046432 HAU/mg**  
**IHA with cholesterol : 98 % - Conforms**


  
**ROXANA MONTEMILONE**      **CHRISTIAN DOMINGUEZ**  
 DIRECTORA TÉCNICA      GERENTE  
 SANOFI PASTEUR S.A.      SANOFI PASTEUR S.A.




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**ADSORBED PURIFIED FHA**

TESTS	SPECIFICATIONS
<b>PURIFIED FHA IN SOLUTION</b>	
PROTEIN CONTENT	350 – 2 100 µg/ml
BACTERIAL ENDOTOXINS	≤ 150 UI/mg of protein
ANTIGENICITY	Specific activity (EU/mg of proteins) ≥ lower confidence limit (P = 0.95) of the specific activity of SP batches
<b>ADSORBED PURIFIED FHA</b>	
ALUMINIUM CONTENT	0.6 - 1.4 mg Al/mg of protein
pH	6.2 - 8.2
FHA IDENTIFICATION	Positive
RESIDUAL DERMONECROTIC ACTIVITY	No necrotic reaction (++++) or marked haemorrhagic reaction (+++) in any of the suckling mice 72h after injection - conforms
BACTERIAL AND FUNGAL STERILITY	No microbial growth

  
 ROXANA MONTEMILONE  
 DIRECTORA TÉCNICA  
 SANOFI PASTEUR S.A.

  
 CHRISTIAN DOMINGUEZ  
 GERENTE  
 SANOFI PASTEUR S.A.





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ADSORBED PURIFIED FHA
Lot Number : FA344108

Date of manufacture : 20.03.2009
Storage temperature : + 5°C ± 3°C
Expiry date : 20 MARCH 2013
Volume : 49.400 liters

PURIFIED FHA IN SOLUTION :

CONTROLS :

Protein content

Method : Spectrophotometry
Date : 17.03.09
Result : 915.01 µg/ml - Conforms

Bacterial endotoxins

Method : LAL
Date : 27.03.09
Result : <5.46 IU/mg of protein

Antigenicity

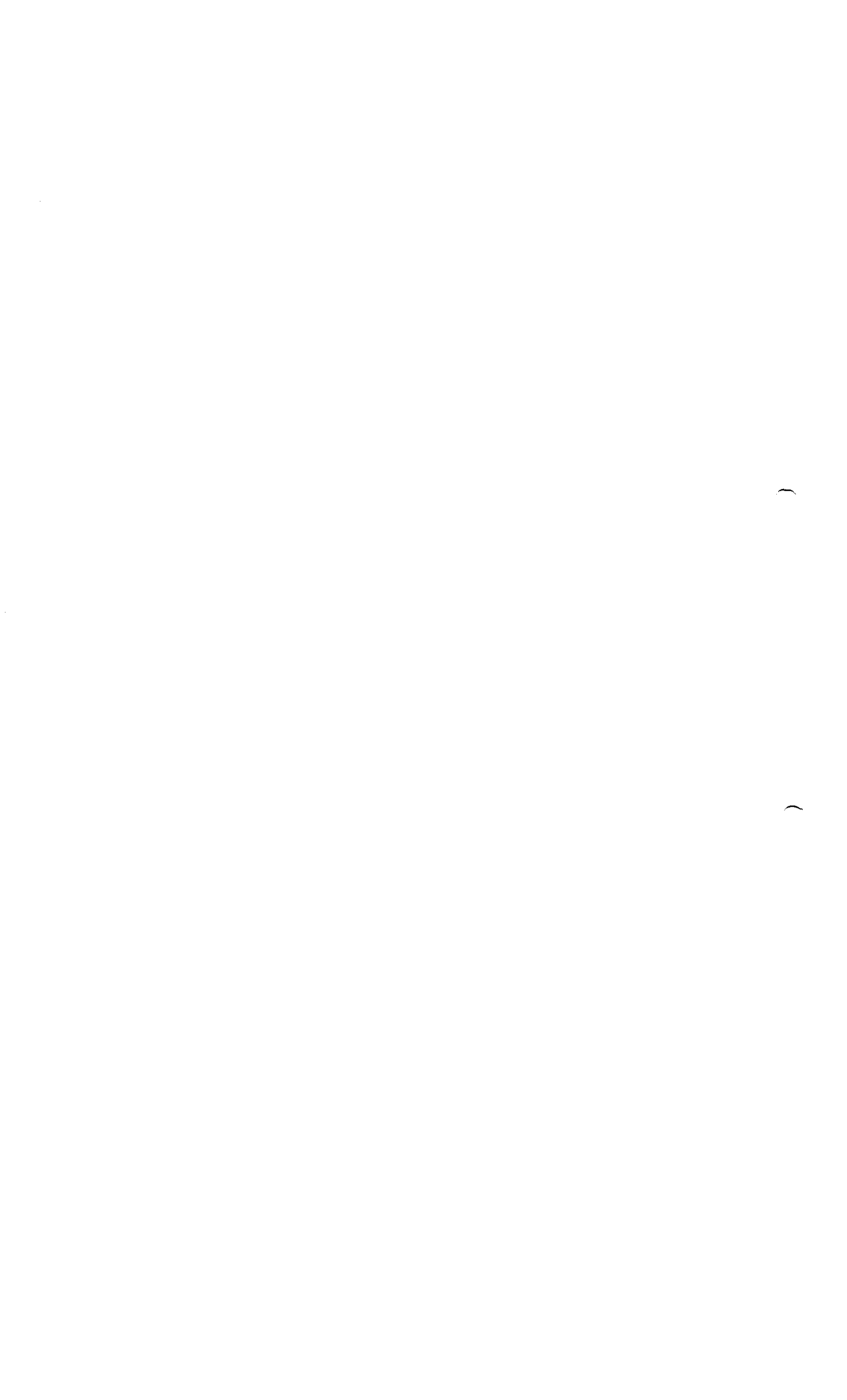
Method : ELISA
Date : 25.03.09

Table with 2 columns: Description and EU/mg of protein. Row 1: Lower confidence limit (P=0.95) of the specific activity of SP batches, 38.5. Row 2: Product, 220.4.

Result : Conforms

Signature of Roxana Montemilone, Directora Técnica, Sanofi Pasteur S.A.

Signature of Christian Dominguez, Gerente, Sanofi Pasteur S.A.



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**ADSORBED PURIFIED FHA :**

**CONTROLS :**

**Aluminium content**

Method : Complexometry  
 Date : 30.03.09  
 Result : 1.03 mg Al/mg of protein – Conforms

**pH**

Method : Glass electrode  
 Date : 30.03.09  
 Result : 7.05 - Conforms

**FHA identification**

Method : Double Diffusion in Gel  
 Date : 31.03.09  
 Result : Positive - Conforms

**Residual dermonecrotic activity**

Method : Specific toxicity  
 Test on : 18.10.10  
 Test off : 21.10.10  
 Result : Conforms

**Bacterial and fungal sterility**

Method	: Membrane filtration	
Media	: Thioglycollate medium	: Soybean Casein Digest medium
Temperatures	: 30-35° C	: 20-25° C
Volume tested	: 20 ml	
Inoculum per Steritest	: 10 ml	: 10 ml
Volume of medium per Steritest	: 100 ml	: 100 ml
Test on	: 24.03.09	
Test off	: 07.04.09	
Result	: No microbial growth - Conforms	

  
 ROXANA MONTEMILONE  
 DIRECTORA TÉCNICA  
 SANOFI PASTEUR S.A.

  
 CHRISTIAN DOMÍNGUEZ  
 GERENTE  
 SANOFI PASTEUR S.A.

