

**sanofi pasteur**

Product Quality and Disposition Department

The vaccines division of sanofi-aventis Group

Diphtheria, tetanus, pertussis (acellular, component),  
 hepatitis B (rDNA), poliomyelitis (inactivated) and Haemophilus  
 influenzae type b conjugate vaccine (adsorbed) lot n° S4312 (clinical batch)

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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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**ADSORBED PURIFIED PERTUSSIS TOXOID**  
**Lot number : FA329595**

Date of manufacture : 18.11.2008  
Storage temperature : + 5°C ± 3°C  
Expiry date : 18 NOVEMBER 2012  
Volume : 35.6 liters

**PURIFIED PERTUSSIS TOXOID IN SOLUTION :**

**CONTROLS :**

**Protein content**

Method : Spectrophotometry  
Date : 14.11.08  
Result : 118.14 µg/ml - **Conforms**

**Bacterial endotoxins**

Method : LAL  
Date : 25.11.08  
Result : 5.33 IU/mg of protein

**Residual glutaraldehyde content**

Method : Spectrophotometry  
Date : 24.11.08  
Result : <2 µg/ml - **Conforms**

**Antigenicity**

Method : ELISA  
Date : 21.11.08

	EU/mg of protein
Lower confidence limit (P=0.95) of the specific activity of SP batches	24.5
Product	60.1

Result : **Conforms**

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**Clustering activity on Chinese Hamster Ovary cells**

Method : Clusters Assay on CHO Cells  
Date : 22.12.08  
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 : 20.02.09

Histamine challenge (Day 5)

Challenge dose per mouse : 2 mg histamine base  
Route : Intraperitoneal  
Date of injection : 25.02.09

Reading date (Day 6) : 26.02.09  
Result (+5°C and +37°C) : ≥ 95% of survival - Conforms

**ADSORBED PURIFIED PERTUSSIS TOXOID :**

**CONTROLS :**

**Aluminium content**

Method : Complexometry  
Date : 25.11.08  
Result : 1.0 mgAl/mg of protein - Conforms

**pH**

Method : Glass electrode  
Date : 25.11.08  
Result : 6.95 - Conforms

**Pertussis identification**

Method : Double diffusion in Gel  
Date : 27.11.08  
Result : Positive - Conforms

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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	:		20.11.08
Test off	:		04.12.08
Result	:	No microbial growth - Conforms	

  
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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 %

  
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**NATIVE PURIFIED FHA**

**Lot number : FA290642**

Date of manufacture : 15.11.2007  
 Storage temperature : + 5°C ± 3°C  
 Expiry date : 15 NOVEMBER 2011  
 Volume : 66.4 liters

**CONTROLS :**

**Protein content**

Method : Spectrophotometry  
 Date : 29.11.07  
 Result : 1364.66 mg/ml

**SDS-page**

Method : Polyacrylamide Gel Electrophoresis  
 Date : 06.12.07  
 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 : 04.12.07  
 Result : Positive - Conforms


**Clustering activity on Chinese Hamster Ovary cells**

Method : Clusters Assay on CHO Cells  
 Date : 12.12.07  
 Result : No cytopathic effect

**Haemagglutinating activity**

Method : Haemagglutination of goose red blood cells by PT  
 Date : 18.12.07  
 Result : 512128 HAU/mg  
 IHA with cholesterol : 97 % - Conforms

  
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 influenzae type b conjugate vaccine (adsorbed) lot n° S4312 (clinical batch)


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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

  
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**ADSORBED PURIFIED FHA**

Lot Number : FA308424

Date of manufacture : 25.04.2008  
 Storage temperature : + 5°C + 3°C  
 Expiry date : 25 APRIL 2012  
 Volume : 54.6 liters

**PURIFIED FHA IN SOLUTION :**

**CONTROLS :**

**Protein content**

Method : Spectrophotometry  
 Date : 22.04.08  
 Result : 1010.84 µg/ml - Conforms

**Bacterial endotoxins**

Method : LAL  
 Date : 29.04.08  
 Result : <4.95 IU/mg of protein

**Antigenicity**

Method : ELISA  
 Date : 22.05.08

	EU/mg of protein
Lower confidence limit (P=0.95) of the specific activity of SP batches	38.5
Product	136.6

Result : Conforms

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**ADSORBED PURIFIED FHA :**

**CONTROLS :**

**Aluminium content**

Method : Complexometry  
Date : 05.05.08  
Result : 1.06 mg Al/mg of protein - Conforms

**pH**

Method : Glass electrode  
Date : 30.04.08  
Result : 6.40 - Conforms

**FHA identification**


Method : Double Diffusion in Gel  
Date : 27.05.08  
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	:	29.04.08
Test off	:	13.05.08
Result	:	No microbial growth - Conforms

  
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**- D - HEPATITIS B**

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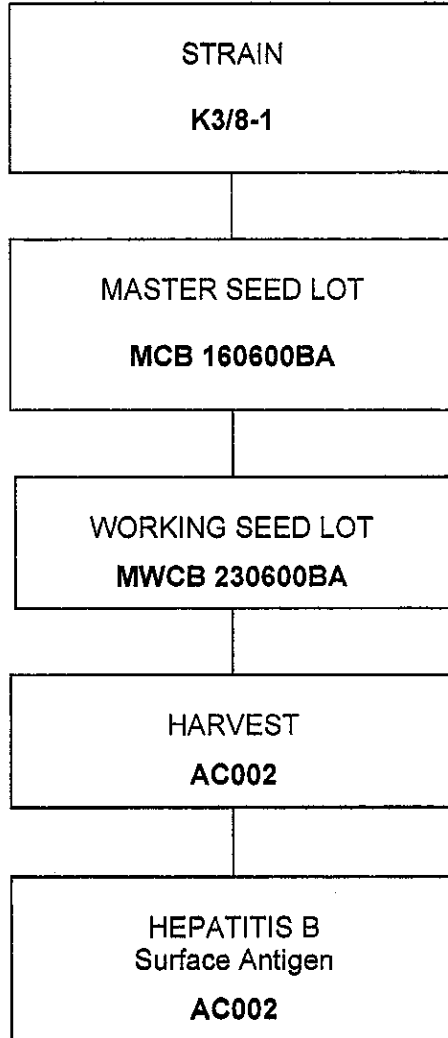
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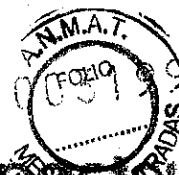
**PRODUCTION FLOW SHEET**

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HANSENULA POLYMORPHA  
Strain : K3/8-1

STRAIN


Name : Hansenula Polymorpha RB11  
Origin : Rhein Biotech  
Received : February 15<sup>th</sup>, 2000


HANSENULA POLYMORPHA  
Master seed lot n° MCB 160600BA

Strain : IM K3/8-1  
Preparation date : June 16<sup>th</sup>, 2000  
Release date : June 29<sup>th</sup>, 2001

CONTROLS

- Purity . **Conforms**
- Identification : **Conforms**
- Full integration of the vector : **Conforms**
- Number of copies of the plasmid in the genome : **Conforms**
- Integrated cDNA gene sequence : **Conforms**
- Sequencing of the regions 3' and 5' : **Conforms**
- Determination of the population of yeast cells containing the cloned gene: **Conforms**

  
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