



sanofi pasteur
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° S4313 (clinical batch) 132/180

MONOVALENT BULK - Type : 1
Lot Number : FA304026

Single harvest used : FA296701 – FA297937
Date of inactivation : 31.03.08
Inactivation method : 0.88% (w/v) Formaldehyde, 37°C, 12 days

Date of manufacture : 31.03.08
Volume : 254 200 ml
Storage temperature : +5°C ± 3°C
Monovalent bulk period of validity : 3 years
Expiry date : 31 MARCH 2011

CONTROLS:

Residual formaldehyde content

Method : Spectrophotometry
Date : 10.04.08
Result : 88.18 µg/ml - Conforms

Protein content

Method : Spectrophotometry
Date : 15.04.08
Result : 21.00 µg/ml

D Antigen content

Method : ELISA
Reference standard : 28.1.99
Date : 03.04.08
Result : 1 364 D Antigen U/ml

Purity

Result : 15.396 ng of protein / D Antigen U - Conforms

[Signatures]
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Bacterial and fungal sterility



Method used	:	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	:	04.04.08
Test off	:	18.04.08
Result	:	No microbial growth

Inactivation kinetics

Method	:	viral titration of polio cytopathogenic effect on sensitive cells
Cell strain used	:	Hep 2
Temperature of incubation	:	36 ± 1°C
Test on	:	04.04.08
Test off	:	11.04.08

TIME	D0	D0 + 24H	D0 + 48H	D0 + 72H	D0 + 96H
Titer (CCID ₅₀ /ml)	10 ^{9.30}	10 ^{5.00}	≤10 ^{2.20}	≤10 ^{1.30}	≤10 ^{1.30}

Slope calculation : - 0.1479, Conforms



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MONOVALENT BULK - Type : 2
Lot Number : FA293397

Single harvest used	: FA286930 – FA287531
Date of inactivation	: 17.12.07
Inactivation method	: 0.88% (w/v) Formaldehyde, 37°C, 12 days
Date of manufacture	: 17.12.07
Volume	: 96 800 ml
Storage temperature	: +5°C ± 3°C
Monovalent bulk period of validity	: 3 years
Expiry date	: 17 DECEMBER 2010

CONTROLS:

Residual formaldehyde content

Method	: Spectrophotometry
Date	: 10.01.08
Result	: 86.59 µg/ml - Conforms

Protein content



Method	: Spectrophotometry
Date	: 08.01.08
Result	: 30.54 µg/ml

D Antigen content

Method	: ELISA
Reference standard	: 28.1.99
Date	: 14.01.08
Result	: 843 D Antigen U/ml

Purity

Result	: 36.2301 ng of protein / D Antigen U - Conforms
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Bacterial and fungal sterility


Method used	:	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	:	20.12.07	
Test off	:	03.01.08	
Result	:	No microbial growth	


Inactivation kinetics

Method	:	viral titration of polio cytopathogenic effect on sensitive cells
Cell strain used	:	Hep 2
Temperature of incubation	:	36 ± 1° C
Test on	:	11.01.08
Test off	:	18.01.08

TIME	D0	D0 + 24H	D0 + 48H	D0 + 72H	D0 + 96H
Titer (CCID ₅₀ /ml)	10 ^{9.60}	10 ^{6.50}	10 ^{3.30}	≤10 ^{1.30}	≤10 ^{1.30}

Slope calculation : - 0.1313, Conforms


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MONOVALENT BULK - Type : 3
Lot Number : FA300586

Single harvest used : FA290835 – FA292974
Date of inactivation : 25.02.08
Inactivation method : 0.88% (w/v) Formaldehyde, 37°C, 12 days

Date of manufacture : 25.02.08
Volume : 207 500 ml
Storage temperature : +5°C ± 3°C
Monovalent bulk period of validity : 3 years
Expiry date : 25 FEBRUARY 2011

CONTROLS:

Residual formaldehyde content

Method : Spectrophotometry
Date : 03.03.08
Result : 85.93 µg/ml - Conforms

Protein content

Method : Spectrophotometry
Date : 04.03.08
Result : 22.67 µg/ml

D Antigen content

Method : ELISA
Reference standard : 28.1.99
Date : 28.02.08
Result : 1 053 D Antigen U/ml

Purity

Result : 21.527 ng of protein / D Antigen U - Conforms

[Signature]
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Bacterial and fungal sterility


Method used	:	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	:	27.02.08
Test off	:	12.03.08
Result	:	No microbial growth


Inactivation kinetics

Method	:	viral titration of polio cytopathogenic effect on sensitive cells
Cell strain used	:	Hep 2
Temperature of incubation	:	36 ± 1°C
Test on	:	29.02.08
Test off	:	07.03.08

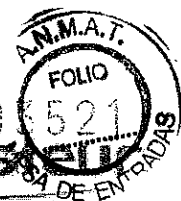
TIME	D0	D0 + 24H	D0 + 48H	D0 + 72H	D0 + 96H
Titer (CCID ₅₀ /ml)	10 ^{9.20}	10 ^{5.30}	≤10 ^{2.00}	≤10 ^{1.30}	≤10 ^{1.30}

Slope calculation : - 0.1500, Conforms


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Test for effective inactivation

Method : Cytopathogenic effect on sensitive cells
Cell strain : Vervet
Volume tested : 3000 theoretical human doses
Virulence challenge : viral suspension (type 1, 2, 3)
about 100-300 CCID₅₀/ml

Temperature of incubation : 37 ± 1°C
Date of inactivation (Day 0) : 13.02.08
Day 9 : 22.02.08
End of inactivation date (Day 12) : 25.02.08

	Inoculation date	Reading date			Result	
		At 7 th day	At 14 th day	At 21 st day		
Day 9	primary test Vervet – V1059	29.04.08	06.05.08	13.05.08	20.05.08	no CPE
	subculture at 7 th day Vervet – V1060	06.05.08		20.05.08		no CPE
	subculture at 14 th day Vervet – V1060	13.05.08		27.05.08		no CPE
	subculture at 21 st day Vervet – V1061	20.05.08		03.06.08		no CPE
	virulence challenge Vervet – V1059	23.05.08		28.05.08		CPE

	Inoculation date	Reading date			Result	
		At 7 th day	At 14 th day	At 21 st day		
Day 12	primary test Vervet – V1060	06.05.08	13.05.08	20.05.08	27.05.08	no CPE
	subculture at 7 th day Vervet – V1061	20.05.08		03.06.08		no CPE
	subculture at 14 th day Vervet – V1061	20.05.08		03.06.08		no CPE
	subculture at 21 st day Vervet – V1062	27.05.08		10.06.08		no CPE
	virulence challenge Vervet – V1060	29.05.08		05.06.08		CPE

Result : No cytopathic effect (CPE)

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CONCENTRATED TRIVALENT BULK

TESTS	SPECIFICATIONS
pH MEASUREMENT	6.8 - 7.5
RESIDUAL FORMALDEHYDE CONTENT	≤ 100 µg/ml
BOVINE SERUM ALBUMINE CONTENT	≤ 100 ng/ml
BACTERIAL ENDOTOXINS CONTENT	≤ 50 IU/ml
BACTERIAL AND FUNGAL STERILITY TEST	No microbial growth
D ANTIGEN CONTENT	
Type 1	240 - 560 D antigen units/ml
Type 2	48 - 112 D antigen units/ml
Type 3	192 - 448 D antigen units/ml
TEST FOR EFFECTIVE INACTIVATION	No cytopathic effect


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CONCENTRATED TRIVALENT BULK
Lot Number : FA328827

Date of manufacture : 07.11.08
Storage temperature : +5°C ± 3°C
Expiry date : 07 NOVEMBER 2010

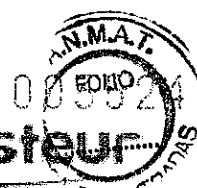
Composition

FORMULA - THEORETICAL COMPOSITION PER ML

Type 1 (MAHONEY) : 400 D units
Type 2 (MEF-1) : 80 D units
Type 3 (SAUKETT) : 320 D units

INGREDIENTS	Lot number	Volume (liter)
Monovalent type 1	FA303359	21.662
	FA304026	68.633
Monovalent type 2	FA293397	28.470
Monovalent type 3	FA300586	91.168
199 Medium	FA318873	90.067
APPROXIMATE TOTAL VOLUME		298.600

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CONTROLS :

pH measurement

Method : Glass electrode
Date : 24.11.08
Result : 7.08 - Conforms

Residual formaldehyde content

Method : Spectrophotometry
Date : 25.11.08
Result : 55.89 µg/ml - Conforms

Bovine serum albumin content

Method : ELISA
Date : 19.11.08
Result : <13.5 ng/ml - Conforms

Bacterial endotoxins content

Method : LAL
Date : 17.11.08
Result : <0.50 IU/ml - Conforms

Bacterial and fungal sterility

Method used	: 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	: 13.11.08	
Test off	: 27.11.08	
Result	: Conforms	


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