

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) 135/180

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

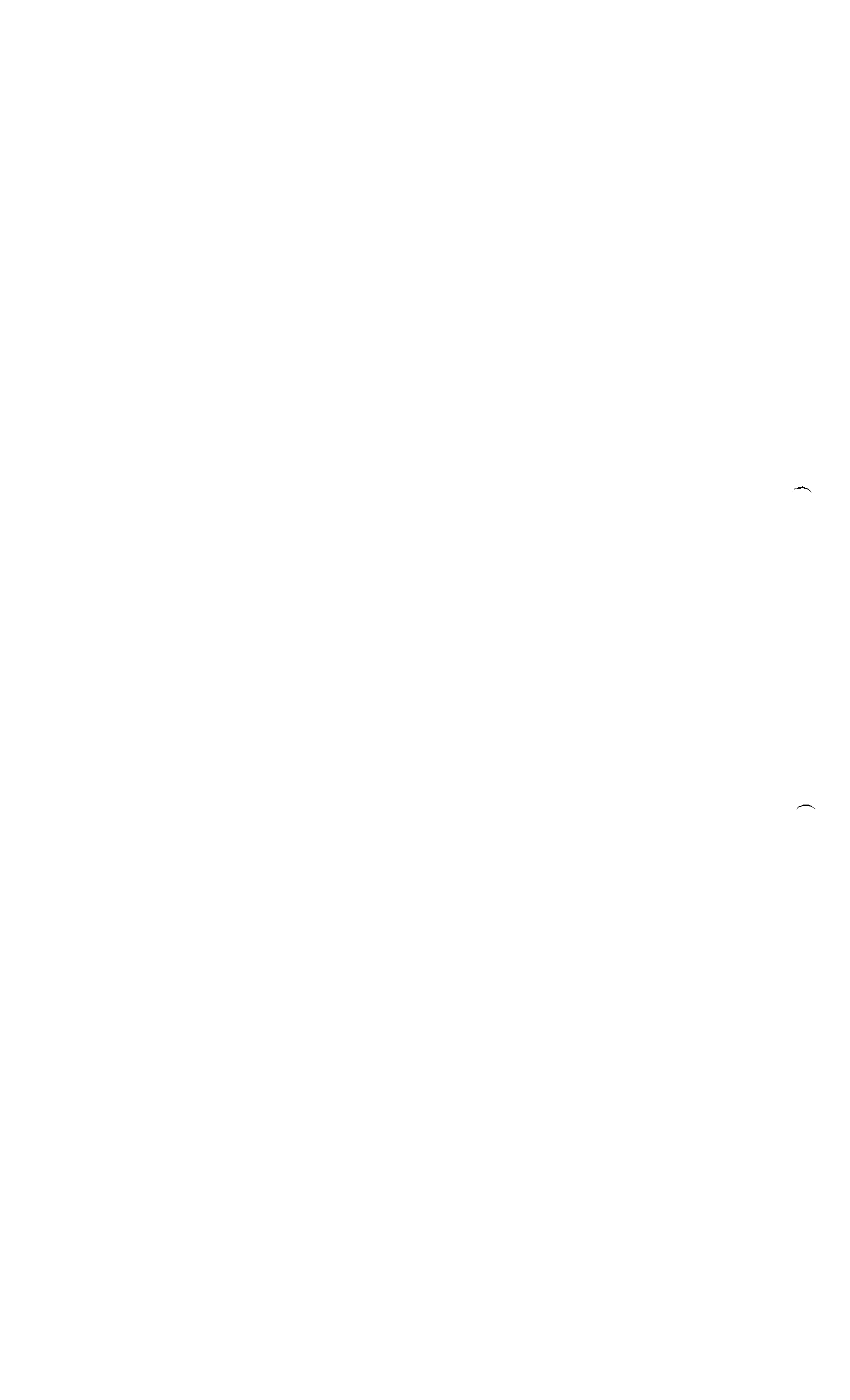
TIME	D0	D0 + 24H	D0 + 48H	D0 + 72H	D0 + 96H
Titer (CCID ₅₀ /ml)	10 ^{9.60}	10 ^{6.50}	10 ^{3.30}	≤10 ^{1.30}	≤10 ^{1.30}

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

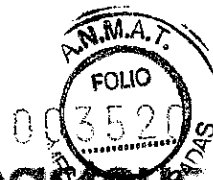
Method	: ELISA
Reference standard	: 28.1.99
Date	: 28.02.08
Result	: 1 053 D Antigen U/ml

Purity

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

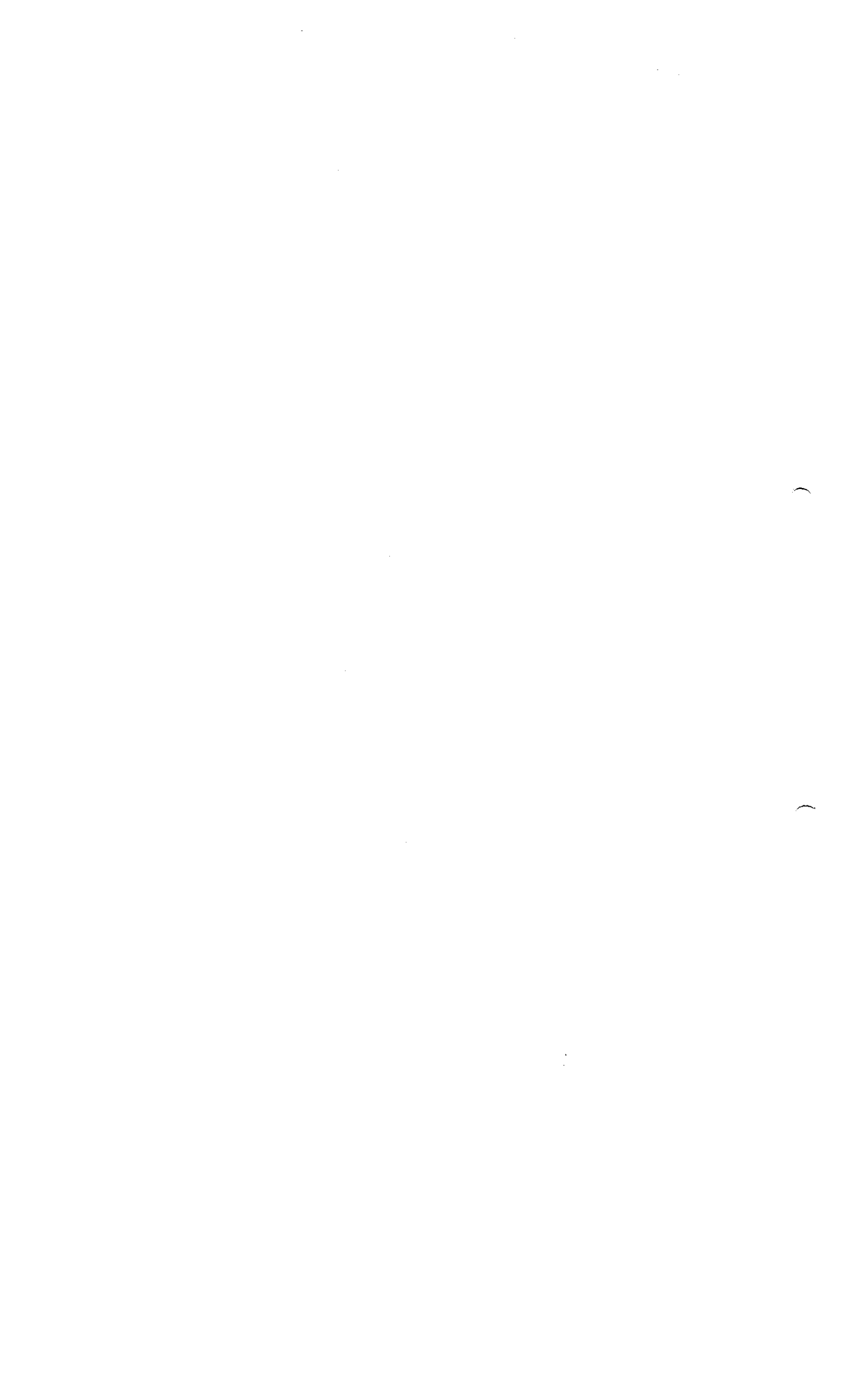
Inactivation kinetics

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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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

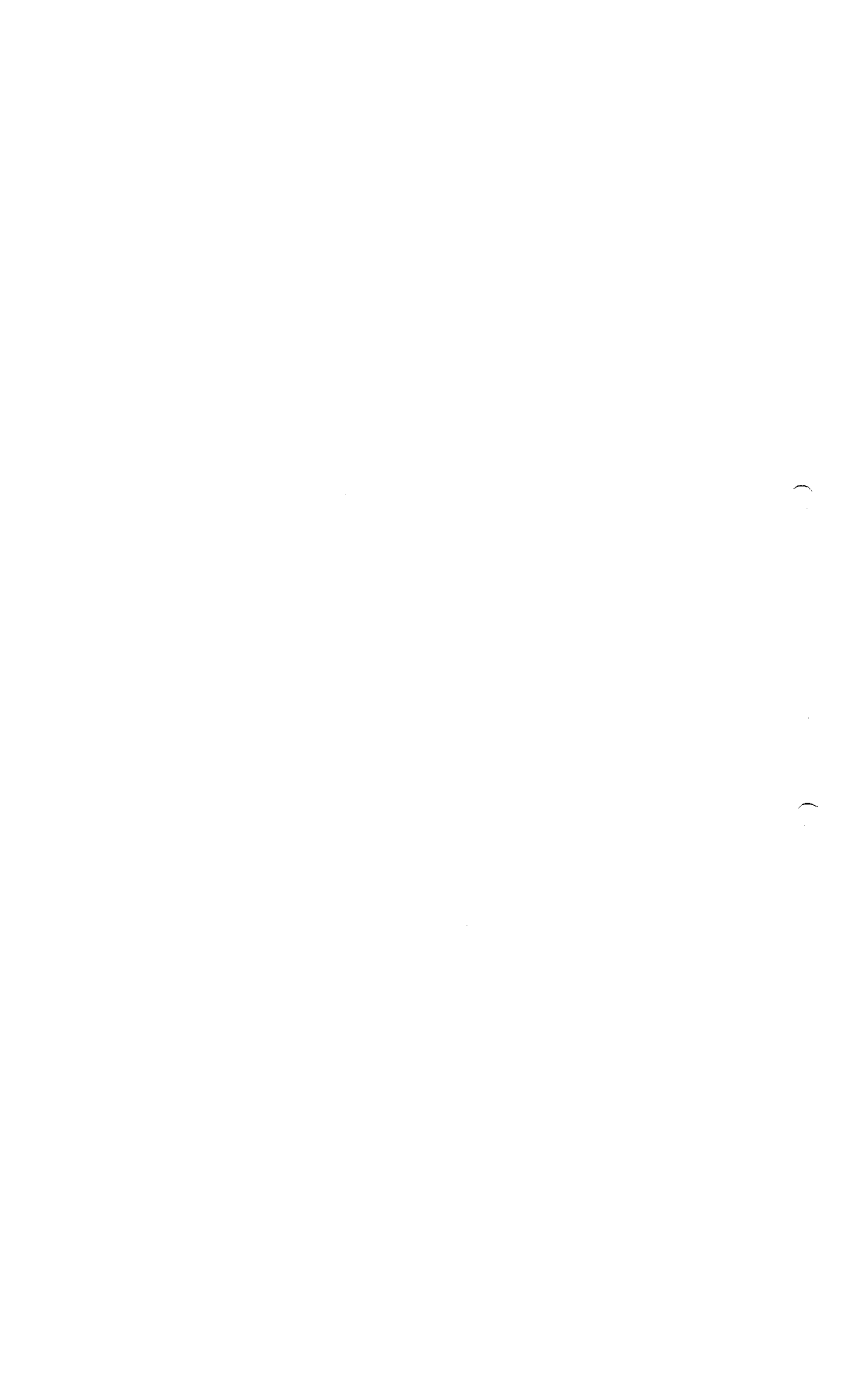
FORMULA - THEORETICAL COMPOSITION PER ML

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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143/180

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

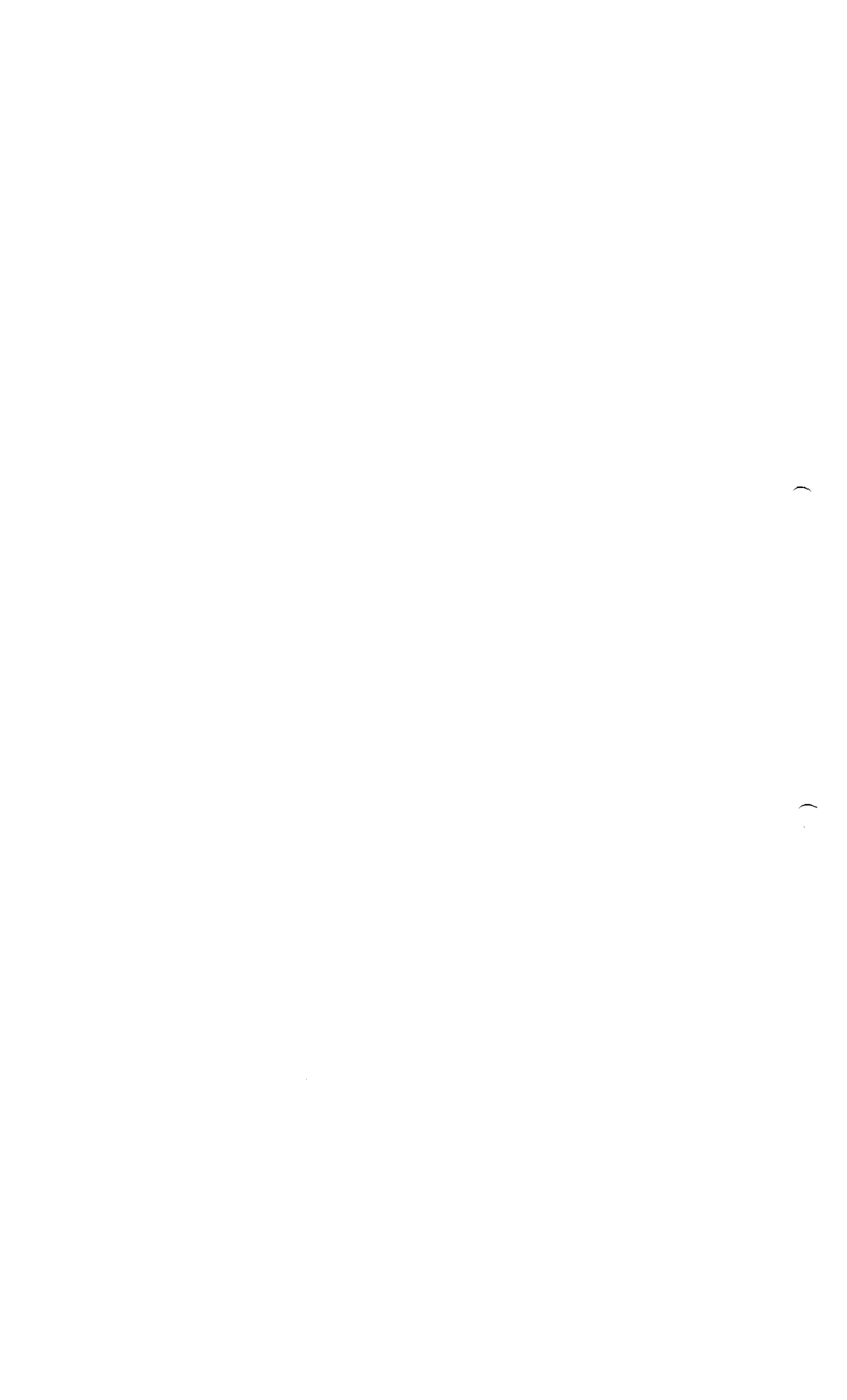
Method used	: Membrane filtration	
Media	: Thioglycollate medium	: Soybean Casein Digest medium
Temperatures	: 30-36° C	: 20-25° C
Volume tested	: 20 ml	
Inoculum per Steritest	: 10 ml	: 10 ml
Volume of medium per Steritest	: 100 ml	: 100 ml
Test on	: 13.11.08	
Test off	: 27.11.08	
Result	: Conforms	



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D Antigen content

Method : ELISA
Reference standard : 11/07/07
Date : 13.11.08

	D Antigen unit/ml		
	Type 1	Type 2	Type 3
Product tested	467	88	339

Result : **Conforms**



Test for effective inactivation

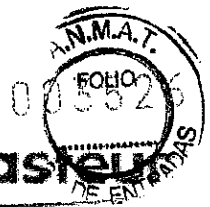
First test

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
Test on : 16.12.08
Test off : 06.01.09

	Inoculation date	Reading date			Result
		At 7 th day	At 14 th day	At 21 st day	
primary test Vervet – V1086	16.12.08	23.12.08	30.12.08	06.01.09	no CPE
subculture at 7 th day Vervet – V1088	15.01.09		30.01.09		no CPE
subculture at 14 th day Vervet – V1088	15.01.09		30.01.09		no CPE
subculture at 21 st day Vervet – V1088	15.01.09		30.01.09		no CPE
virulence challenge Vervet – V1086	07.01.09		14.01.09		CPE

Result : **No cytopathic effect (CPE)**


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Second test

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
 Test on : 13.01.09
 Test off : 03.02.09

	Inoculation date	Reading date			Result
		At 7 th day	At 14 th day	At 21 st day	
primary test Vervet – V1087	13.01.09	20.01.09	27.01.09	03.02.09	no CPE
subculture at 7 th day Vervet – V1088	20.01.09		03.02.09		no CPE
subculture at 14 th day Vervet – V1088	27.01.09		10.02.09		no CPE
subculture at 21 st day Vervet – V1091	03.02.09		17.02.09		no CPE
virulence challenge Vervet – V1087	05.02.09	12.02.09			CPE

Result : No cytopathic effect (CPE)


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