

Additional information on lot - INFLUENZA VACCINE (SPLIT VIRION. INACTIVATED)

Bacterial and Fungal Sterility

Method	Membrane filtration	
	Thioglycollate medium	Soybean Casein Digest medium
Media		
Temperatures	30-35°C	20-25°C
Volume tested	ml	
Inoculum per steritest	ml	ml
Volume of medium per steritest	100 ml	100 ml
Number of inoculated steritest	1	1
Test on		
Test off		
Result		

RESIDUAL INFECTIOUS VIRUS

Method	Research for live virus into embryonated chicken eggs
First inoculation	
Date	
Inoculated dilutions (log10)	pure, -1, -2
Volume inoculated by egg	ml
Number of inoculated eggs by dilution	
Incubation period and temperature	hours at °C
Date of egg cooling	
Date of harvest and mixture of allantoic fluids (AF) for each dilution	
Harvest storage	+5 +/-3°C
Second inoculation	
Date	
Volume of AF inoculated by egg	ml from each previous dilution

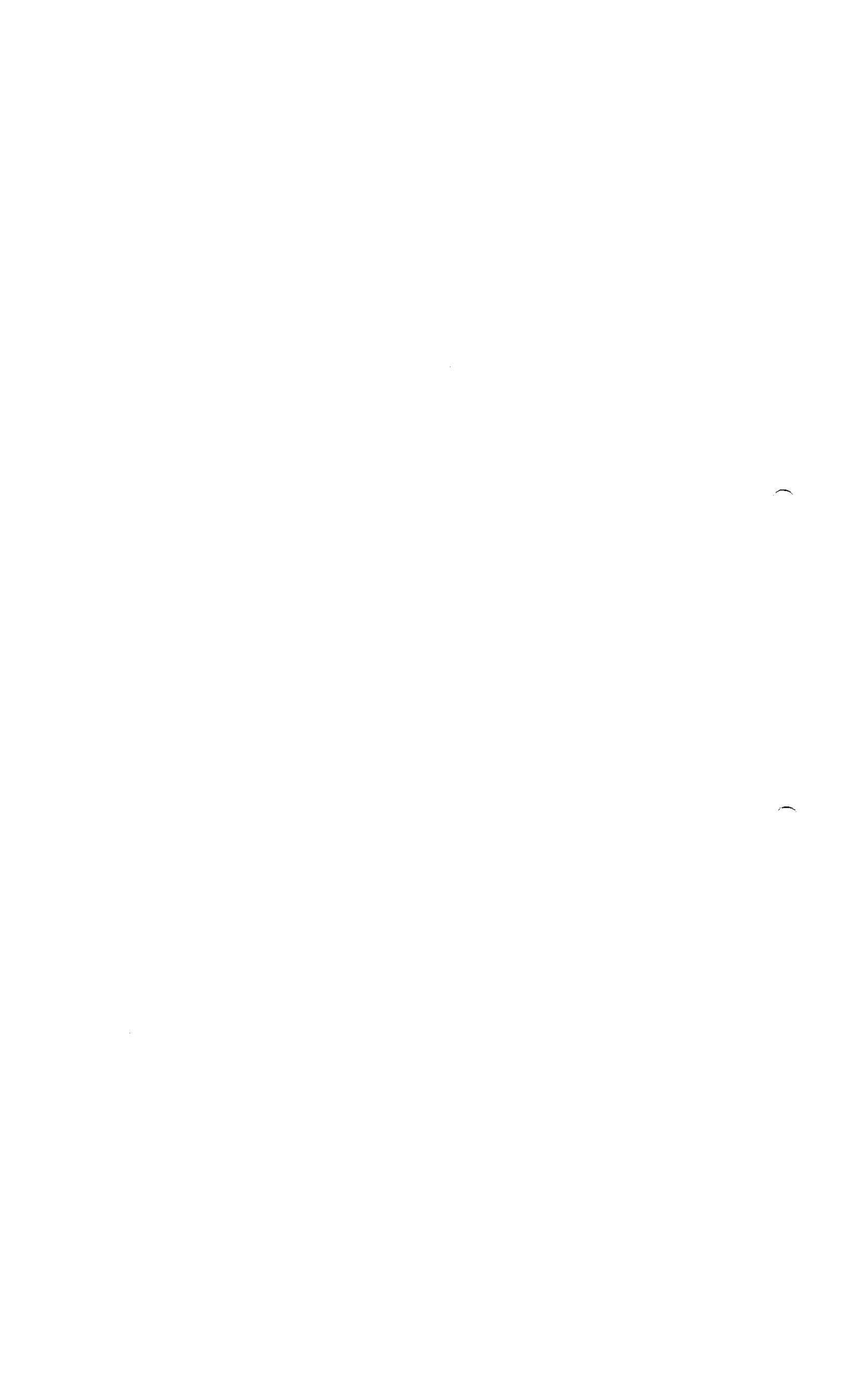
Destinataire : A l'attention de l'ANSM
 Export officiel non contrôlé
 Motif : Batch REUSE PRODUIT

Information Confidentielle
Page 58 de 70

ROXANA MONTEMILONE
DIRECTORA TECNICA
APODERADA
SANOFI PASTEUR S. A.
Número : Q_0565202
Version : 2.0
Categoría : I

Par : BOSSUT Isabelle
Le : 24 oct. 2016 13:56:56

Statut : Applicable





Haemagglutinin Antigen Identification

Method Haemagglutination inhibition test
Date

Antisera used : = B/Yamagata lineage
= A/H1N1
= A/H3N2
= B/Victoria lineage

Antigens used : = B/Yamagata lineage
= A/H1N1
= A/H3N2
= B/Victoria lineage

Result:

ANTIGEN	ANTISERA			
	ANTI B/Yamagata	ANTI H1 A/	ANTI H3 A/	ANTI B/Victoria
B/Yamagata				
A/H1N1				
A/H3N2				
B/Victoria				
BULK				

Conclusion

Destinatario : A Fattention de YANISM

Export officiel non contrôlé
Motif : Batch Release Product QV...

Information Confidentielle
Page 60 de 70

Par : BOSSUT Isabelle
Le : 24 oct. 2016 13:56:56

Statut : Applicable

ROXANA MONTEMLONE
DIRECTORA TECNICA
APODERADA
SANOFI PASTEUR S.A
Número : Q_0565202
Version : 2.0
Categoría : I





**INFLUENZA VACCINE (SPLIT VIRION,
INACTIVATED) MONOVALENT POOLED
HARVEST**

ORIGINAL STRAIN B/ Yamagata lineage

Working virus seed lot used :

PRODUCTION

Dates of inoculation, harvest, disruption and inactivation

Inoculation	Harvest	Disruption	Inactivation

Disruption agent : Octoxynol 9
Treatment ≥ 1 hour

Storage conditions before inactivation : + 5° ± 3°C

Inactivation : By formaldehyde action

Concentration of inactivating agent : 0.2 %

Time of inactivation : 25-26 hours at +20°C +/- 5°C followed by a stage at +5°C +/- 3°C for 24-96 hours

Storage conditions after inactivation : + 5° ± 3°C

Concentration and purification procedure

Isopycnic ultracentrifugation on a saccharose gradient

Antibiotics used during preparation : Neomycine sulfate in the inoculum

Filtration : On 0.22 µm pore size membrane

Destinatario : A Fattention de FANSM

Export officiel non contrôlé
Mórti : Batch Release protocol QIV





Certificate of Analysis

Product Name : INFLUENZA VACCINE (SPLIT VIRION, INACTIVATED)

Process Stage : WORKING SEED LOT

Volume / Quantity :

Storage Condition : ≤ -60°C

Date of Manufacture :

Working Seed Lot

Test(s)	Acceptance Criteria	Result	Approval Date
TEST FOR MYCOPLASMA BY MICROBIOLOGICAL CULTURE <i>By Inoculation to suitable culture media</i>	Negative for the presence of mycoplasma when cultured on agar and broth		
BACTERIAL AND FUNGAL STERILITY <i>By Membrane filtration</i>	No microbial growth		
TEST FOR MYCOPLASMA BY EPIFLUORESCENCE IN CELLULAR CULTURE <i>By Inoculation to indicator cells and specific staining</i>	Negative for the presence of mycoplasma when cultured in cells and treated with a fluorescent dye		
NEURAMINIDASE ANTIGEN IDENTIFICATION <i>By RT-PCR</i>	POSITIVE		
HAEMAGGLUTININ ANTIGEN IDENTIFICATION <i>By Haemagglutination inhibition</i>	POSITIVE		
INFECTIOUS TITER <i>By EID50</i>	≥ 6 log10 EID50/mL	log10 EID50/mL	

Export officiel non contrôlé
Motif : Batch release process

Information Confidentielle
Page 62 de 70

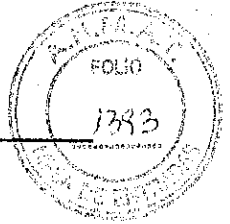
ROXANA MONTEMILONE
DIRECTORA TÉCNICA
APODERADA
SANOFI PASTEUR S.A.

Par : BOSSUT Isabelle
Le : 24 oct. 2016 13:56:56

Statut : Applicable

Numéro : Q_0565202
Version : 2.0
Catégorie : 1





INFLUENZA VACCINE (SPLIT VIRION, INACTIVATED)
WORKING VIRUS SEED LOT
B/Yamagata lineage -

A/ PRODUCTION

Lot number :

Inoculation

Date of inoculation :

Inoculum : Primary seed lot

Passage number from primary seed lot :

Inoculated dilution (log10) :

Eggs used :

Inoculated volume per egg : mL

Number of eggs inoculated :

Temperature of incubation : **Optimal incubation conditions**

Added antibiotics : None

Harvest and purification

Date :

Storage conditions : ≤ - 60°C

Release date :

Destinataire : A l'attention de l'ANSM

Export officiel non contrôlé
Marr: Batch Release Protocol QV 14-2016

Information Confidentielle
Page 63 de 70

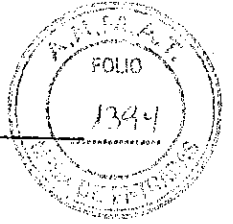
ROXANA MONTEMLONE
DIRECTORA TÉCNICA
APODERADA
SANOFI PASTEUR S.A.

Par : BOSSUT Isabelle
Le : 24 oct. 2016 13:56:56

Statut : Applicable

Numéro : Q_0565202
Version : 2.0
Catégorie : 1





B – CONTROLS

Test for mycoplasma

- by culture method

Method : Agar culture

Volume tested : ml

Media used : Hayflick – Frey

Temperature of incubation :

Positive controls :
Mycoplasma pneumoniae, Mycoplasma
orale, Mycoplasma gallisepticum,
Mycoplasma synoviae, Acholeplasma
laidlawii

. Test on :

. Test off :

Subculture at the 3rd day

. Test on :

. Test off :

Subculture at the 7th day

. Test on :

. Test off :

Subculture at the 14th day

. Test on :

. Test off :

Subculture at the 21th day

. Test on :

. Test off :

Result :

Positive control :

Mycoplasma pneumoniae :

Mycoplasma orale :

Mycoplasma gallisepticum :

Mycoplasma synoviae :

Acholeplasma laidlawii :

Result :

Destinataire : A l'attention de l'ANSM

Export officiel non contrôlé
Motif : Batch Release pour exportation

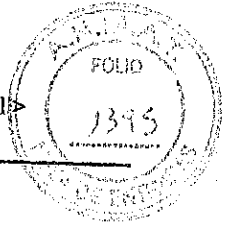
Information Confidentielle
Page 64 de 70

ROXANA MONTEMILONE
DIRECTORA TÉCNICA
APODERADA
SANOFI PASTEUR S.A.

Par : BOSSUT Isabelle
Le : 24 oct. 2016 13:56:56

Statut : Applicable

Numéro : Q_0565202
Version : 2.0
Catégorie : 1



**Test for Mycoplasma
- by epifluorescence in cell culture**

Method : DNA fluorescence staining
 Cell used : ,th passage
 Volume tested : ml
 Temperature of incubation : °C
 Positive control : Mycoplasma hyorhinitis and Mycoplasma orale
 Test on :
 Test off :
 Result :

Bacterial and fungal sterility

Method : Membrane filtration

Media	Thioglycollate medium	Soybean Casein Digest medium
Temperatures	30-35°C	20-25°C
Volume tested	ml	ml
Inoculum per Steritest	100 ml	100 ml
Volume of medium	1	1
Number of inoculated Steritest		
Test on		
Test off		
Result		

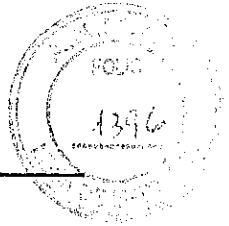
Destinataire : A l'attention de l'ANSM
 Export officiel non contrôlé
 Motif : Batch release procedure

Information Confidentielle
Page 65 de 70

ROXANA MONTEMILONE
 DIRECTORA TÉCNICA
 APODERADA
 SANOFI PASTEUR S.A.
 Numéro : Q_0565202
 Version : 2.0
 Catégorie : 1

Par : BOSSUT Isabelle
 Le : 24 oct. 2016 13:56:56

Statut : Applicable



Haemagglutinin Antigen Identification

Method Haemagglutination inhibition test
Date

Antisera used : = B/Yamagata lineage
 = A/H1N1
 = A/H3N2
 = B/Victoria lineage

Antigens used : = B/Yamagata lineage
 = A/H1N1
 = A/H3N2
 = B/Victoria lineage

Result:

ANTIGEN	ANTISERA			
	ANTI B/Yamagata	ANTI H1 A/	ANTI H3 A/	ANTI B/Victoria
B/Yamagata				
A/H1N1				
A/H3N2				
B/Victoria				
WORKING VIRUS SEED LOT				

Conclusion

Destinataire : A l'attention de l'ANSM

Export officiel non contrôlé
Matière : Bactériologie / microbiologie

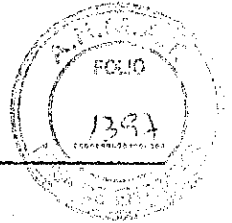
Information Confidentielle
Page 66 de 70

ROXANA MONTEMILONE
DIRECTORA TECNICA
APODERADA
SANOFI PASTEUR S.A.

Par : BOSSUT Isabelle
Le : 24 oct. 2016 13:56:56

Statut : Applicable

Numéro : Q_0565202
Version : 2.0
Catégorie : I



Infectious titer

Method : Haemagglutination (HA) System
used : Embryonated hen eggs Number
of tests :
Test on : Test
off :

Virus concentration per ml
expressed in log 10 : and Infectious Dose 50/ml

Mean of the titers : Infectious Dose 50/ml

Destinatario : A. Facultad de FANSM

Export oficial non controlé
Motif : Batch RELEASE PRODUCE

Information Confidencielle
Page 67 de 70

ROXANA MONTEMILONE
DIRECTORA TÉCNICA
APODERADA
SANOFI PASTEUR S.A.

Par : BOSSUT Isabelle
Le : 24 oct. 2016 13:56:56

Statut : Applicable

Numéro : Q_0565202
Version : 2.0
Catégorie : 1



Certificate of Analysis

Product Name : INFLUENZA VACCINE (SPLIT VIRION. INACTIVATED)

Process Stage : PRIMARY SEED LOT

Volume / Quantity :

Storage Condition : ≤ -60°C

Date of Manufacture :

Master Seed Lot

Test(s)	Acceptance Criteria	Result	Approval Date
HAEMAGGLUTININ ANTIGEN IDENTIFICATION <i>By Haemagglutination inhibition</i>	POSITIVE		

Destinataire : A l'attention de l'ANSM

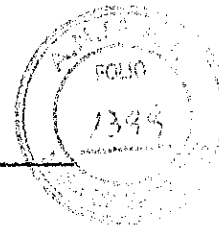
Export officiel non contrôlé
Modif : Batch Release protocol QIV

Information Confidentielle
Page 68 de 70

Par : BOSSUT Isabelle
Le : 24 oct. 2016 13:56:56

Statut : Applicable

ROXANA MONTEMILONE
DIRECTORA TECNICA
APODERADA
SANOFI PASTEUR Q_0565202
Version : 2.0
Catégorie : 1



**INFLUENZA VACCINE (SPLIT VIRION, INACTIVATED)
MASTER VIRUS SEED LOT

ORIGINAL STRAIN**

Name : B/Yamagata lineage
Origin :
Lot number :
Received :
Passage history on receipt :

**MASTER VIRUS SEED LOT
A - PRODUCTION**

Lot number :

Inoculation

Date of inoculation :
Passage number from reassortant received :
Dilutions of inoculum (log10) :
Eggs used :
Number of eggs per dilution :
Inoculated volume per egg : ml
Temperature of incubation : °C

Harvest of allantoic fluids

Date of harvest :
Pool of allantoic fluids at the dilution (log10) :
Filling and storage at $\leq - 60^{\circ}\text{C}$

Release date :

Destinataire : A l'attention de l'ANSM

Export officiel non contrôlé
Motif : Batch Release protocol Q/V

Information Confidentielle
Page 69 de 70

ROXANA MONTEMILONE
DIRECTORA TÉCNICA
APODERADA
SANOFI PASTEUR S.A.

Par : BOSSUT Isabelle
Le : 24 oct. 2016 13:56:56

Statut : Applicable

Numéro : Q_0565202
Version : 2.0
Catégorie : I



B - CONTROLS

Haemagglutinin Antigen Identification

Method Haemagglutination inhibition test

Date

Antisera used : = B/Yamagata lineage
= A/H1N1
= A/H3N2
= B/Victoria lineage

Antigens used : = B/Yamagata lineage
= A/H1N1
= A/H3N2
= B/Victoria lineage

Result:

ANTIGEN	ANTISERA			
	ANTI B/Yamagata	ANTI H1 A/	ANTI H3 A/	ANTI B/Victoria
B/Yamagata				
A/H1N1				
A/H3N2				
B/Victoria				
MASTER VIRUS SEED LOT				

Destinataire : A. Latamien de l'ANM

Conclusion

Export officiel non contrôlé
Motif : Bacul'Venue 180880707-1-14

Information Confidentielle
Page 70 de 70

ROXANA MONTEMILONE
DIRECTORA TECNICA
APODERADA
SANOFI PASTEUR S.A.

Par : BOSSUT Isabelle
Le : 24 oct. 2016 13:56:56

Statut : Applicable

Numéro : Q_0565202
Version : 2.0
Catégorie : 1

