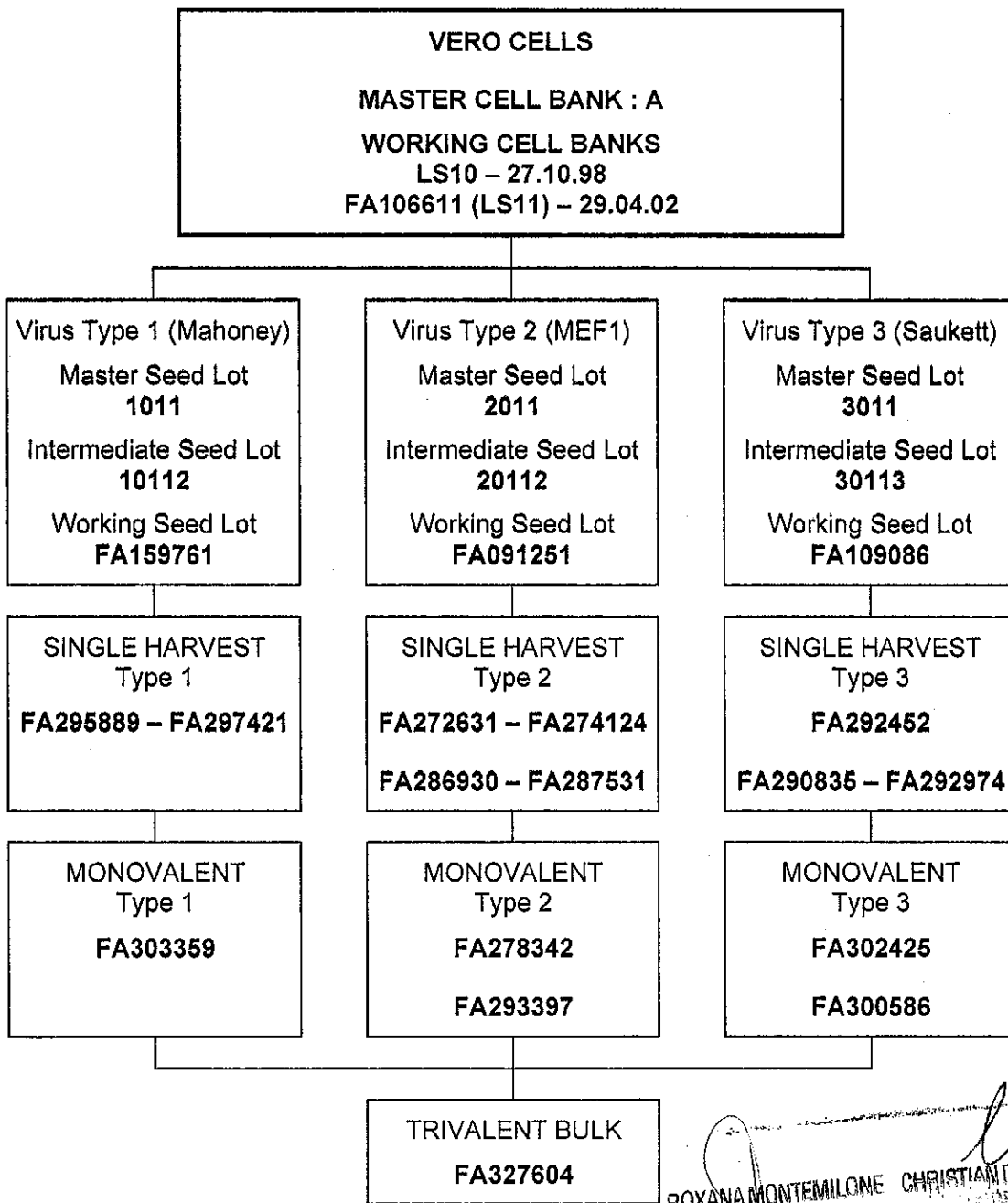



Product Quality and Disposition Department


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

68/229

PRODUCTION FLOW SHEET




ROXANA MONTEMILONE
 DIRECTORA TÉCNICA
 SANOFI PASTEUR S.A.


CHRISTIAN DOMÍNGUEZ
 GERENTE
 SANOFI PASTEUR S.A.





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° S4312 (clinical batch) 69/229

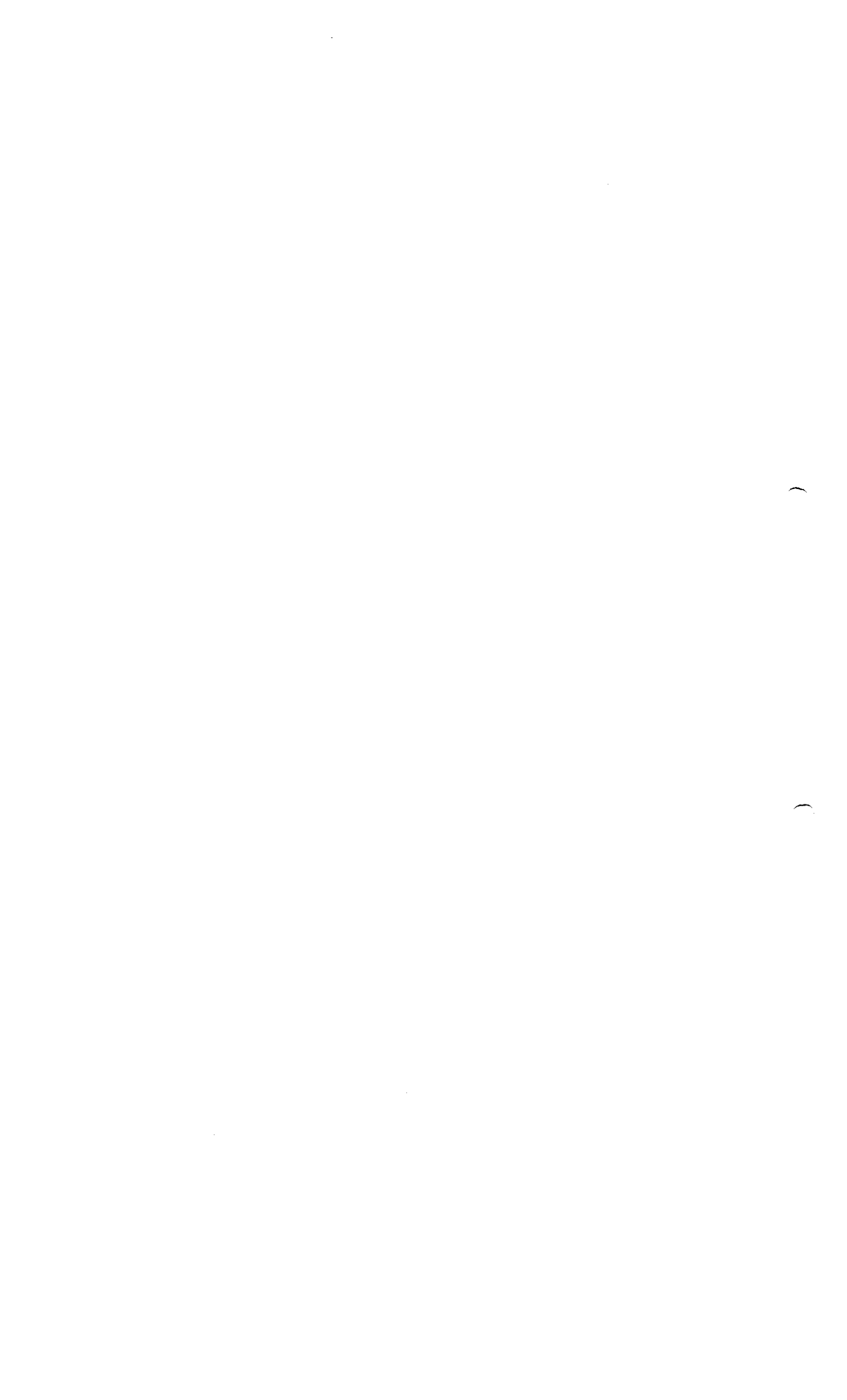
POLIOMYELITIS VACCINE (INACTIVATED)
MASTER CELL BANK -VERO CELLS-
Lot Number : A

Strain Cell : Cercopithecus aethiops kidney cells.
Supplier : American Type Culture Collection
Reference : ATCC-CCL 81 at 124th passage
Received : 22.05.79
Aventis Pasteur reference : ATCC-CCL 81 VERO F1415

Master Cell Bank:
Aventis Pasteur reference : Cell Bank A at 129th passage
Preparation date : 21.06.79
Storage temperature : liquid nitrogen


ROXANA MONTEMILONE
DIRECTORA TÉCNICA
SANOFI PASTEUR S.A.


CHRISTIAN DOMÍNGUEZ
CODERADO
SANOFI PASTEUR S.A.



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° S4312 (clinical batch)


70/229


POLIOMYELITIS VACCINE (INACTIVATED)
 WORKING CELL BANK -VERO CELLS-
 Lot Number : **LS10**

Master Cell Bank : Cell Bank A at 129th passage

Working Cell Bank :

Aventis Pasteur reference : **LS10** at 137th passage
 Preparation date : **27.10.98**
 Release date : **18.12.00**
 Storage temperature : liquid nitrogen


ROXANA MONTEMILONE
 DIRECTORA TÉCNICA
 SANOFI PASTEUR S.A.


CHRISTIAN DOMÍNGUEZ
 GERENTE
 SANOFI PASTEUR S.A.



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° S4312 (clinical batch)


71/229


POLIOMYELITIS VACCINE (INACTIVATED)
WORKING CELL BANK -VERO CELLS-
Lot Number : FA106611 (LS11)

Master Cell Bank : Cell Bank A at 129th passage

Working Cell Bank :

Aventis Pasteur reference : FA106611 (LS11) at 137th passage
Preparation date : 29.04.02
Release date : 26.03.08
Storage temperature : liquid nitrogen


ROXANA MONTEMILONE
DIRECTORA TÉCNICA
SANOFI PASTEUR S.A.


CHRISTIAN DOMÍNGUEZ
GERENTE
SANOFI PASTEUR S.A.



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° S4312 (clinical batch) 72/229

POLIOMYELITIS VACCINE (INACTIVATED)
 MASTER VIRUS SEED LOT - Type 1
 Lot Number 1011

| | |
|------------------------|--|
| Virus strain | : MAHONEY type 1 |
| Original strain | : 74/3-B3 - Pitman and Moore Company |
| Supplier | : RIJKS Instituut Voor de Volksgezondheid (RIV) Bilthoven - Netherlands |
| Received from supplier | : 04.02.77 |
| Cells used | : Primary Monkey kidney cells of Erythrocebus Patas |
| Preparation date | : 09.03.77 |
| Release date | : 02.09.77 |

POLIOMYELITIS VACCINE (INACTIVATED)
 INTERMEDIATE VIRUS SEED LOT - Type 1
 Lot Number 10112

| | |
|------------------|--|
| Master seed lot | : 1011 |
| Cells used | : Primary Monkey kidney cells of Erythrocebus Patas |
| Preparation date | : 17.05.79 |
| Release date | : 26.09.79 |

| | |
|--|---|
|  ROXANA MONTEMILONE DIRECTORA TÉCNICA SANOFI PASTEUR S.A. |  CHRISTIAN DOMINGUEZ PRODERADO SANOFI PASTEUR S.A. |
|--|---|



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° S4312 (clinical batch) 73/229


POLIOMYELITIS VACCINE (INACTIVATED)
MASTER VIRUS SEED LOT - Type 2
Lot Number 2011

Virus strain : MEF 1 type 2
Original strain : 68/2-B3 - Statens Serum Institute, Copenhagen
Supplier : RIJKS Instituut Voor de Volksgezondheid (RIV)
Bilthoven - Netherlands
Received from supplier : 04.02.77
Cells used : Primary Monkey kidney cells of **Erythrocebus Patas**
Preparation date : 09.03.77
Release date : 02.09.77

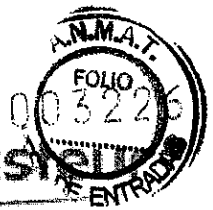
POLIOMYELITIS VACCINE (INACTIVATED)
INTERMEDIATE VIRUS SEED LOT - Type 2
Lot Number 20112

Master seed lot : 2011
Cells used : Primary Monkey kidney cells of **Erythrocebus Patas**
Preparation date : 07.05.79
Release date : 26.09.79


ROXANA MONTEMILONE
DIRECTORA TÉCNICA
SANOFI PASTEUR S.A.


CHRISTIAN DOMÍNGUEZ
GERENTE
SANOFI PASTEUR S.A.





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° S4312 (clinical batch) 74/229

POLIOMYELITIS VACCINE (INACTIVATED)
MASTER VIRUS SEED LOT - Type 3
Lot Number 3011

Virus strain : SAUKETT type 3
Original strain : 74/2-B2 - Statens Serum Institute, Copenhagen
Supplier : RIJKS Instituut Voor de Volksgezondheid (RIV)
Bilthoven - Netherlands
Received from supplier : 04.02.77
Cells used : Primary Monkey kidney cells of **Erythrocebus Patas**
Preparation date : 09.03.77
Release date : 03.11.77

POLIOMYELITIS VACCINE (INACTIVATED)
INTERMEDIATE VIRUS SEED LOT - Type 3
Lot Number 30113

Master seed lot : 3011
Cells used : Primary Monkey kidney cells of **Erythrocebus Patas**
Preparation date : 18.05.79
Release date : 15.10.79

ROXANA MONTEMILONE
DIRECTORA TÉCNICA
SANOFI PASTEUR S.A.

CHRISTIAN DOMÍNGUEZ
AFIDUADO
SANOFI PASTEUR S.A.





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° S4312 (clinical batch)


75/229


POLIOMYELITIS VACCINE (INACTIVATED)
WORKING VIRUS SEED LOT - Type : 1
Lot Number : FA159761

Working Cell Bank : LS10

Intermediate seed lot : 10112

Working seed lot : FA159761
Cell amplification from 137th to 142nd passage : 07.08.03 to 28.08.03
Number of passage between PSL and WSL : 2
Preparation date : 09.09.03
Release date : 15.04.04
Storage temperature : ≤ -35°C


ROXANA MONTEMILONE
DIRECTORA TÉCNICA
SANOFI PASTEUR S.A.


CHRISTIAN DOMÍNGUEZ
ENCARGADO
SANOFI PASTEUR S.A.





Product Quality and Disposition Department.

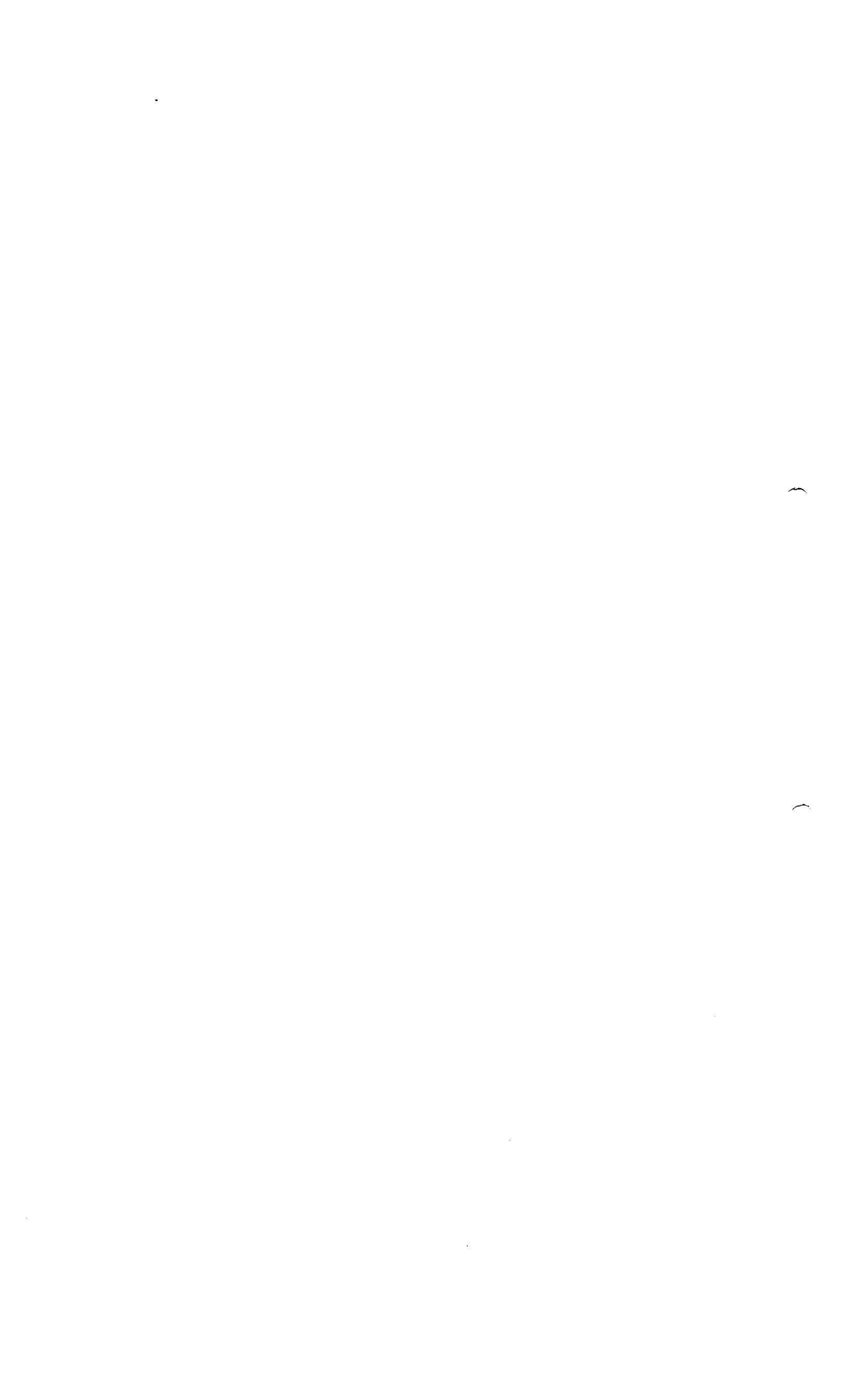
Diphtheria, tetanus, pertussis (acellular, component),
hepatitis B (rDNA), poliomyelitis (inactivated) and Haemophilus
influenzae type b conjugate vaccine (adsorbed) lot n° S4312 (clinical batch) 76/229

POLIOMYELITIS VACCINE (INACTIVATED)
WORKING VIRUS SEED LOT - Type : 2
Lot Number : FA091251

Working Cell Bank : LS10
Intermediate seed lot : 20112
Working seed lot : FA091251
Cell amplification from 137th to 142nd passage : 13.09.01 to 04.10.01
Number of passage between PSL and WSL : 2
Preparation date : 16.10.01
Release date : 30.05.02
Storage temperature : ≤ -35° C


ROXANA MONTEMILONE
DIRECTORA TÉCNICA
SANOFI PASTEUR S.A.

CHRISTIAN DOMÍNGUEZ
ENCUADERADO
SANOFI PASTEUR S.A.





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° S4312 (clinical batch)

77/229

POLIOMYELITIS VACCINE (INACTIVATED)
WORKING VIRUS SEED LOT - Type : 3
Lot Number : **FA109086**

Working Cell Bank : LS10

Intermediate seed lot : 30113

Working seed lot : FA109086

Cell amplification from 137th to 142nd passage : 14.03.02 to 03.04.02

Number of passage between PSL and WSL : 2

Preparation date : 17.04.02

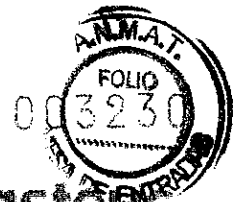
Release date : 09.01.03

Storage temperature : ≤ -35°C


ROXANA MONTEMILONE
DIRECTORA TÉCNICA
SANOFI PASTEUR S.A.


CHRISTIAN DOMÍNGUEZ
GERENTE
SANOFI PASTEUR S.A.





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)

78/229

SINGLE HARVEST (TYPE 1, 2 AND 3)

| TESTS | ACCEPTANCE CRITERIA |
|---|--|
| ON CELLS | |
| OBSERVATION | Absence of cytopathic effect due to extraneous agents |
| TEST FOR HAEMADSORBING VIRUSES | Absence of hemadsorption |
| SIMIAN CELLS IDENTIFICATION | Positive identification |
| ON SUPERNATANT | |
| TEST FOR EXTRANEIOUS AGENTS USING CELLS . VERO CELLS . HUMAN DIPLOID CELLS . PRIMARY MONKEY KIDNEY CELLS | Absence of cytopathic effect for each cell type |
| TEST FOR MYCOPLASMA BY CULTURE METHOD | No growth of mycoplasma |
| TEST FOR MYCOPLASMA BY EPIFLUORESCENCE IN CELL CULTURE | No mycoplasma detected by epifluorescence in cell culture |
| SINGLE VIRUS HARVEST | |
| POLIO VIRUS IDENTIFICATION | Positive |
| POLIO VIRUS CONCENTRATION | $\geq 10^7$ CCID ₅₀ /ml |
| BACTERIAL AND FUNGAL STERILITY | No microbial growth |
| TEST FOR MYCOPLASMA BY CULTURE METHOD | No growth of mycoplasma |
| CONCENTRATED PURIFIED VIRAL SUSPENSION | |
| PROTEIN CONTENT | For purity ratio calculation |
| D ANTIGEN CONTENT | For purity ratio calculation |
| BACTERIAL AND FUNGAL STERILITY | No microbial growth |
| PURITY (SPECIFIC ACTIVITY) | Type 1 : < 0.027 µg of protein/D antigen unit Type 2 : < 0.0875 µg of protein/D antigen unit Type 3 : < 0.030 µg of protein/D antigen unit |

ROXANA MONTEMILONE, CHRISTIAN DOMINIQUEZ
 DIRECTORA TECNICA, JEFE DE AREA
 SANOFI PASTEUR S.A. SANOFI PASTEUR S.A.

1

2



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° S4312 (clinical batch) 79/229

SINGLE HARVEST - Type : 1
Lot Number : FA295889

CELL:

Working Cell Bank : FA106611
Date of thawing ampoule of WCB : 13.12.07
Thawing ampoule amount : One ampoule

VIRUS:

Virus Working Seed lot : FA159761
Date of inoculation : 07.01.08
Date of virus harvest : 09.01.08

CRUDE HARVEST:

Storage : from 11.01.08 to 14.01.08
Volume : 1 493 L
Storage temperature : +5°C ± 3°C

SINGLE HARVEST:


Date of single harvest : 14.01.08


CONCENTRATION AND PURIFICATION OF THE SINGLE HARVEST

DEAE Spherodex large column : ion exchange chromatography on 15.01.08
CL-6-B Sepharose column : Gel filtration on 16.01.08
DEAE Sphérodex small column : ion exchange chromatography on 16.01.08

CONCENTRATED PURIFIED VIRAL SUSPENSION :

Manufacture date : 16.01.08
Volume : 19 600 ml
Storage temperature : +5°C ± 3°C


ROXANA MONTEMILONE
DIRECTORA TÉCNICA
SANOFI PASTEUR S.A.


CHRISTIAN DOMINGUEZ
ENCUADRADO
SANOFI PASTEUR S.A.



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° S4312 (clinical batch) 80/229**

CONTROLS ON CELLS:

Observation


Method : Studied through a microscope
 Cells : Vero, 142nd passage
 Number of cells tested : 320*10⁶ cells
 Test on : 07.01.08
 Test off : 21.01.08
 Result : **Absence of cytopathic effect**


Test for haemadsorbing viruses

Method : visual inspection
 Number of vials tested : 8
 Type of red blood cells : Guinea-pig
 Incubation : 4 vials, 30 minutes at 5°C ± 3°C
 : 4 vials, 30 minutes at 20-25°C
 Date : 21.01.08
 Result : **Absence of hemadsorption**

Simian cells identification

Method : Isoenzymes analysis by IsoElectric Focusing
 Iso-enzymes analysed : Lactate DeHydrogenase
 Phospho Gluconate Dehydrogenase
 Glucose Phosphate Isomerase
 Reference cells : Vero, MRC5, WI38, Hep 2
 Date : 03.04.08
 Result : **Positive identification**


 ROXANA MONTEMILONE
 DIRECTORA TÉCNICA
 SANOFI PASTEUR S.A.


 CHRISTIAN DOMINGUEZ
 COORDINADOR
 SANOFI PASTEUR S.A.





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° S4312 (clinical batch)

81/229

CONTROLS ON SUPERNATANTS:

Test for extraneous agents

Vero cells

| | |
|---------------------------|---------------------------------------|
| Method | : Studied through a microscope |
| Type of cells | : Vero |
| Volume tested | : 10 ml |
| Temperature of incubation | : 36 ± 1° C |
| Test on | : 29.01.08 |
| Test off | : 12.02.08 |
| Result | : Absence of cytopathic effect |

Human diploid cells

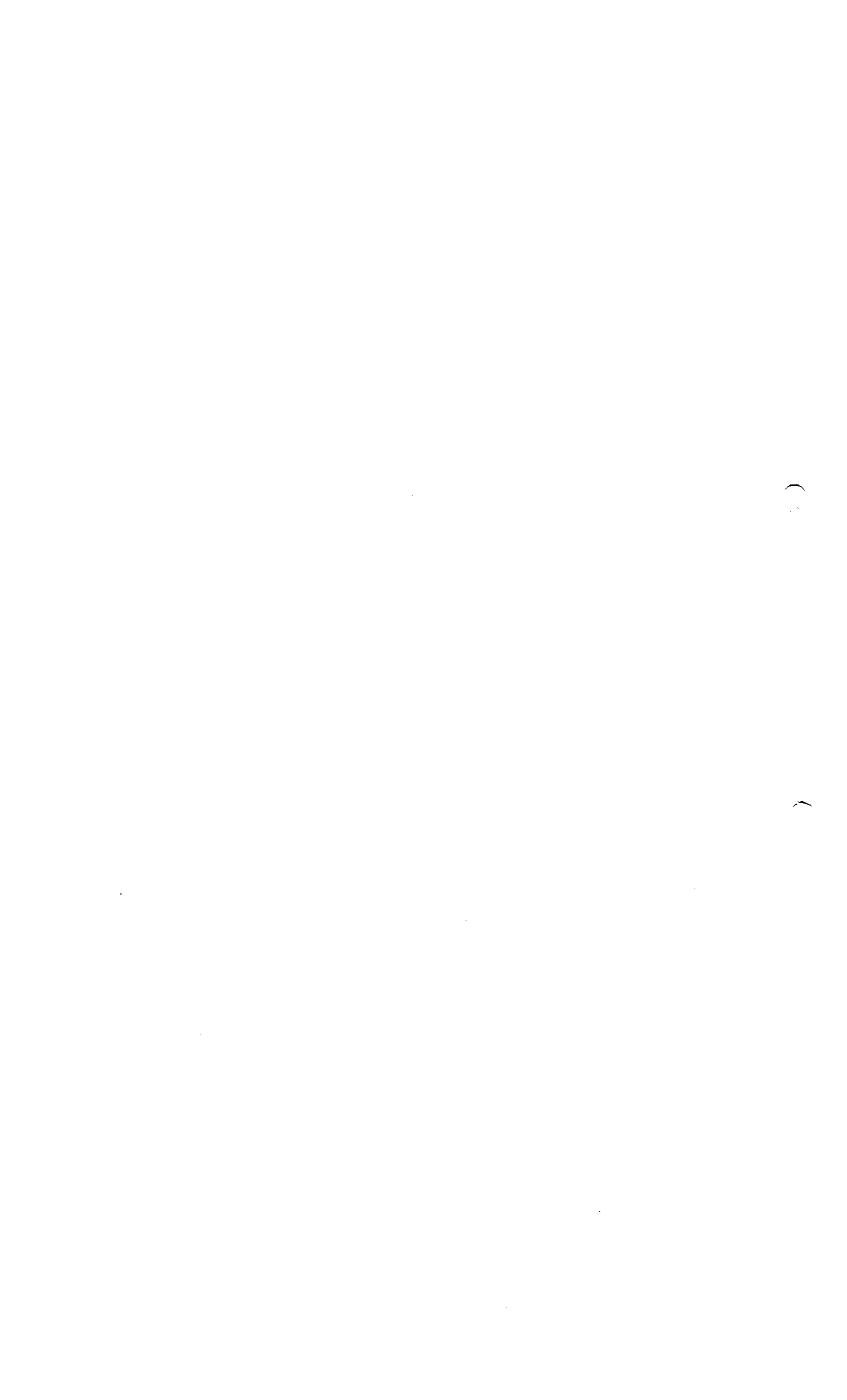
| | |
|---------------------------|---------------------------------------|
| Method | : Studied through a microscope |
| Type of cells | : MRC5 |
| Volume tested | : 10 ml |
| Temperature of incubation | : 36 ± 1° C |
| Test on | : 20.02.08 |
| Test off | : 19.03.08 |
| Result | : Absence of cytopathic effect |

Primary monkey kidney cells

| | |
|---------------------------|---------------------------------------|
| Method | : Studied through a microscope |
| Type of cells | : Vervet Monkey Cells |
| Volume tested | : 10 ml |
| Temperature of incubation | : 36 ± 1° C |
| Test on | : 12.02.08 |
| Test off | : 26.02.08 |
| Result | : Absence of cytopathic effect |


 ROXANA MONTEMILONE
 DIRECTORA TÉCNICA
 SANOFI PASTEUR S.A.


 CHRISTIAN DOMÍNGUEZ
 GERENTE
 SANOFI PASTEUR S.A.



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° S4312 (clinical batch)



82/229

Test for Mycoplasma by culture method

| | |
|--|--|
| Method | : Agar culture |
| Volume tested | : 34 ml |
| Media used | : Hayflick solid Hayflick semi-solid B.O.B. solid B.O.B. semi-solid |
| Temperature of incubation | : 36 ± 1° C |
| Positive controls | : <i>M. pneumoniae</i> and <i>M. orale</i> and <i>A. laidlawii</i> |
| <i>Primary test</i> | |
| Test on | : 20.10.08 |
| Test off | : 03.11.08 |
| <i>Subculture at 3rd day</i> | |
| Test on | : 23.10.08 |
| Test off | : 06.11.08 |
| <i>Subculture at 7th day</i> | |
| Test on | : 27.10.08 |
| Test off | : 12.11.08 |
| <i>Subculture at 14th day</i> | |
| Test on | : 03.11.08 |
| Test off | : 17.11.08 |
| <i>Subculture at 21th day</i> | |
| Test on | : 10.11.08 |
| Test off | : 17.11.08 |
| Result | : No growth of Mycoplasma |

Test for Mycoplasma by epifluorescence in cell culture

| | |
|---------------------------|--|
| Method | : DNA fluorescence staining |
| Cell used | : Vero, 152 nd passage |
| Volume tested | : 1 ml |
| Temperature of incubation | : 36 ± 1° C |
| Positive control | : <i>M. hyorhinis</i> and <i>M. orale</i> |
| Test on | : 10.04.08 |
| Test off | : 17.04.08 |
| Result | : No Mycoplasma detected by epifluorescence in cell culture |

| | |
|---|--|
|  ROXANA MONTEMILONE DIRECTORA TÉCNICA SANOFI PASTEUR S.A. |  CHRISTIAN DOMINGUEZ COORDINADOR SANOFI PASTEUR S.A. |
|---|--|



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° S4312 (clinical batch) 83/229

CONTROLS ON SINGLE VIRUS HARVEST:

Polio virus identification



Method : Cytopathogenic effect neutralization
Cell strain used : Hep 2
Antiserum : MAHONEY type 1
Test on : 23.07.08
Test off : 30.07.08
Result : Positive

Polio virus concentration

Method : Cytopathogenic effect on sensitive cells
Cell strain used : Hep 2
Test on : 23.07.08
Test off : 30.07.08
Virus concentration : 10^{8.97} CCID₅₀/ml
Result : 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 | : | 16.01.08 | |
| Test off | : | 30.01.08 | |
| Result | : | No microbial growth | |

| | |
|---|---|
|  |  |
| ROXANA MONTEMILONE DIRECTORA TÉCNICA SANOFI PASTEUR S.A. | CHRISTIAN DOMINGUEZ COORDINADOR SANOFI PASTEUR S.A. |





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° S4312 (clinical batch)

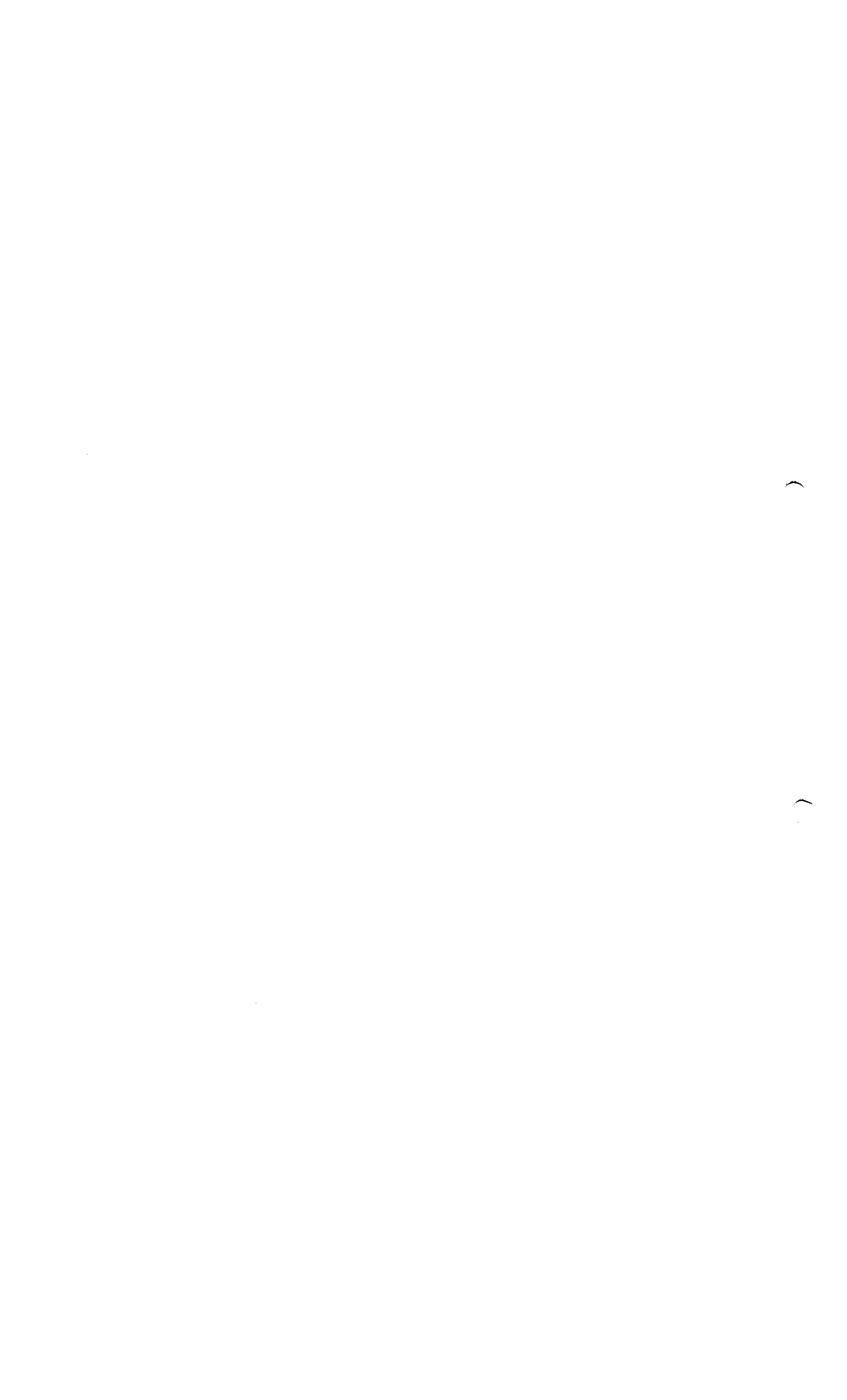
84/229

Test for Mycoplasma by culture method

| | |
|--|--|
| Method | : Agar culture |
| Volume tested | : 34 ml |
| Media used | : Hayflick solid Hayflick semi-solid B.O.B. solid B.O.B. semi-solid |
| Temperature of incubation | : 36 ± 1° C |
| Positive controls | : <i>M. pneumoniae</i> and <i>M. orale</i> and <i>A. laidlawii</i> |
| | |
| <i>Primary test</i> | |
| Test on | : 20.10.08 |
| Test off | : 03.11.08 |
| <i>Subculture at 3rd day</i> | |
| Test on | : 23.10.08 |
| Test off | : 06.11.08 |
| <i>Subculture at 7th day</i> | |
| Test on | : 27.10.08 |
| Test off | : 12.11.08 |
| <i>Subculture at 14th day</i> | |
| Test on | : 03.11.08 |
| Test off | : 17.11.08 |
| <i>Subculture at 21th day</i> | |
| Test on | : 10.11.08 |
| Test off | : 17.11.08 |
| Result | : No growth of Mycoplasma |


 ROXANA MONTEMILONE
 DIRECTORA TÉCNICA
 SANOFI PASTEUR S.A.


 CHRISTIAN DOMINGUEZ
 COORDENADO
 SANOFI PASTEUR S.A.



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° S4312 (clinical batch)**

85/229

CONTROLS ON CONCENTRATED PURIFIED VIRAL SUSPENSION :

Protein content

Method : Spectrophotometry
 Date : 12.02.08
 Result : 105.90 µg/ml

D Antigen content


Method : ELISA
 Reference standard : 28.1.99
 Date : 21.01.08
 Result : 11 915 D Antigen U/ml

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 | : | 21.01.08 | |
| Test off | : | 04.02.08 | |
| Result | : | No microbial growth | |

Purity

Result : 0.009 µg of protein / D Antigen U



 ROXANA MONTEMILONE
 DIRECTORA TÉCNICA
 SANOFI PASTEUR S.A.



 CHRISTIAN DOMÍNGUEZ
 SUPERVISOR
 SANOFI PASTEUR S.A.





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° S4312 (clinical batch) 86/229

SINGLE HARVEST - Type : 1
Lot Number : FA297421

CELL:

Working Cell Bank : FA106611
Date of thawing ampoule of WCB : 27.12.07
Thawing ampoule amount : One ampoule

VIRUS:

Virus Working Seed lot : FA159761
Date of inoculation : 21.01.08
Date of virus harvest : 23.01.08

CRUDE HARVEST:

Storage : from 25.01.08 to 28.01.08
Volume : 1 486 L
Storage temperature : +5°C ± 3°C

SINGLE HARVEST:

Date of single harvest : 28.01.08

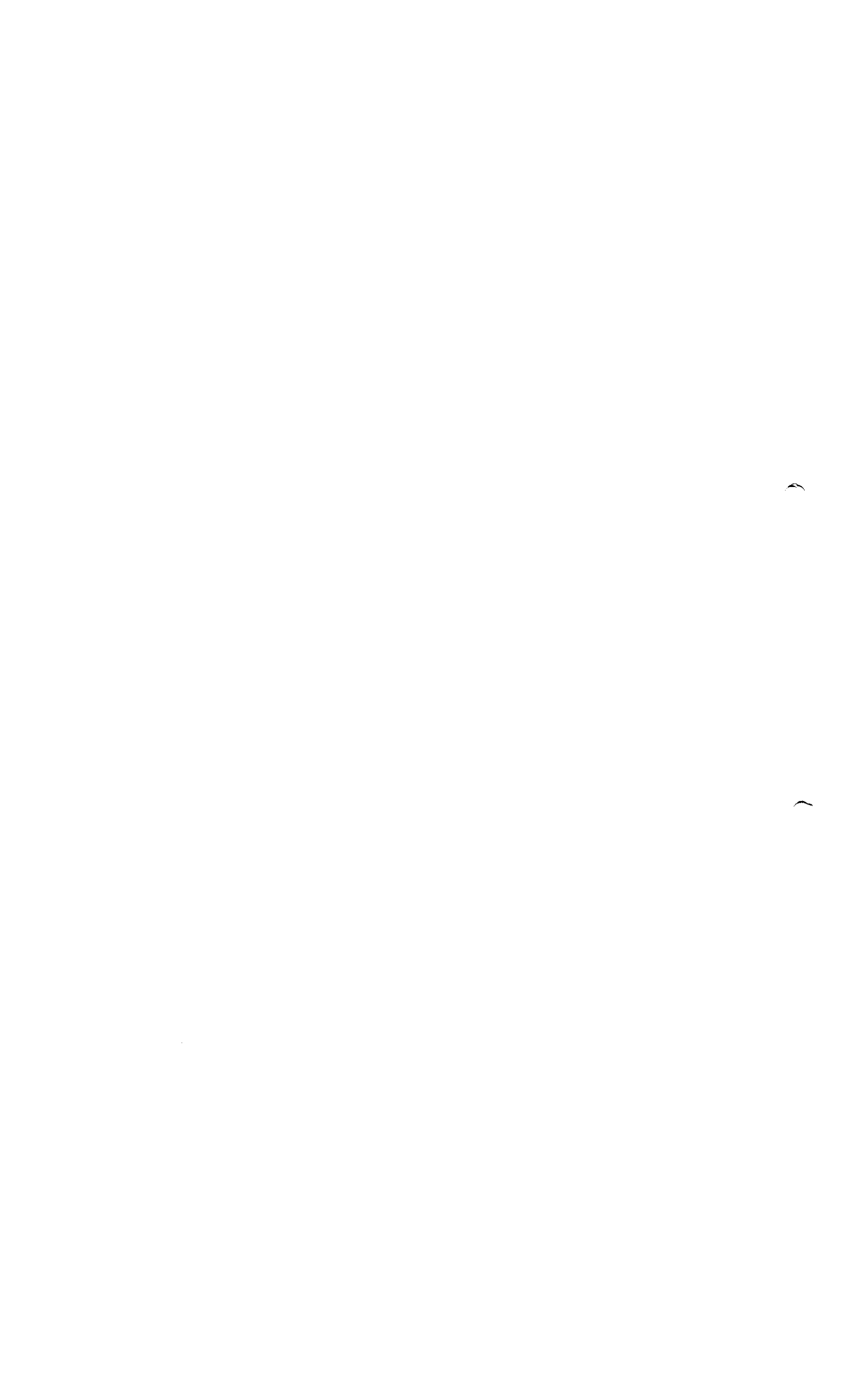
CONCENTRATION AND PURIFICATION OF THE SINGLE HARVEST

DEAE Spherodex large column : Ion exchange chromatography on 29.01.08
CL-6-B Sepharose column : Gel filtration on 30.01.08
DEAE Sphérodex small column : Ion exchange chromatography on 30.01.08

CONCENTRATED PURIFIED VIRAL SUSPENSION :

Manufacture date : 30.01.08
Volume : 19 400 ml
Storage temperature : +5°C ± 3°C

ROXANA MONTEMILONE DIRECTORA TÉCNICA SANOFI PASTEUR S.A.
CHRISTIAN DOMÍNGUEZ SUPERADGO SANOFI PASTEUR S.A.





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° S4312 (clinical batch)

87/229

CONTROLS ON CELLS:

Observation



| | |
|------------------------|-----------------------------------|
| Method | : Studied through a microscope |
| Cells | : Vero, 142 nd passage |
| Number of cells tested | : 320*10 ⁶ cells |
| Test on | : 21.01.08 |
| Test off | : 04.02.08 |
| Result | : Absence of cytopathic effect |

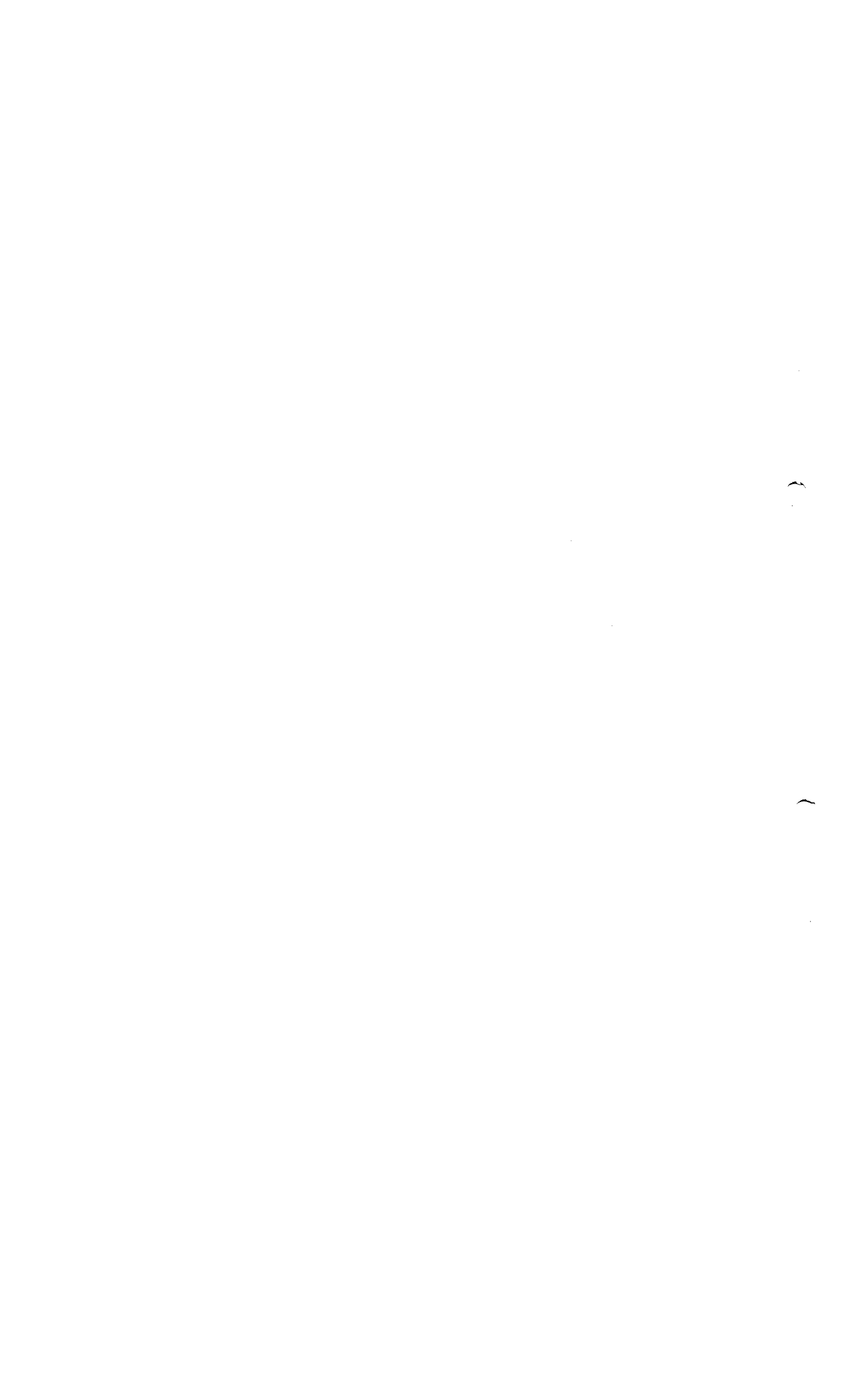
Test for haemadsorbing viruses

| | |
|-------------------------|------------------------------------|
| Method | : visual inspection |
| Number of vials tested | : 8 |
| Type of red blood cells | : Guinea-pig |
| Incubation | : 4 vials, 30 minutes at 5°C ± 3°C |
| | : 4 vials, 30 minutes at 20-25°C |
| Date | : 04.02.08 |
| Result | : Absence of hemadsorption |

Simian cells identification

| | |
|----------------------|---|
| Method | : Isoenzymes analysis by IsoElectric Focusing |
| Iso-enzymes analysed | : Lactate DeHydrogenase Phospho Gluconate Dehydrogenase Glucose Phosphate Isomerase |
| Reference cells | : Vero, MRC5, WI38, Hep 2 |
| Date | : 30.06.08 |
| Result | : Positive Identification |

| | |
|---|---|
|  |  |
| ROXANA MONTEMILONE DIRECTORA TÉCNICA SANOFI PASTEUR S.A. | CHRISTIAN DOMINGUEZ CONTRADO SANOFI PASTEUR S.A. |





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)

88/229

CONTROLS ON SUPERNATANTS:

Test for extraneous agents

Vero cells

| | |
|---------------------------|--------------------------------|
| Method | : Studied through a microscope |
| Type of cells | : Vero |
| Volume tested | : 10 ml |
| Temperature of incubation | : 36 ± 1° C |
| Test on | : 10.03.08 |
| Test off | : 25.03.08 |
| Result | : Absence of cytopathic effect |

Human diploid cells

| | |
|---------------------------|--------------------------------|
| Method | : Studied through a microscope |
| Type of cells | : MRC5 |
| Volume tested | : 10 ml |
| Temperature of incubation | : 36 ± 1° C |
| Test on | : 11.03.08 |
| Test off | : 08.04.08 |
| Result | : Absence of cytopathic effect |

Primary monkey kidney cells

| | |
|---------------------------|--------------------------------|
| Method | : Studied through a microscope |
| Type of cells | : Vervet Monkey Cells |
| Volume tested | : 10 ml |
| Temperature of incubation | : 36 ± 1° C |
| Test on | : 12.02.08 |
| Test off | : 26.02.08 |
| Result | : Absence of cytopathic effect |


 ROXANA MONTEMILONE
 DIRECTORA TÉCNICA
 SANOFI PASTEUR S.A.


 CHRISTIAN DOMINGUEZ
 SUPERVISOR
 SANOFI PASTEUR S.A.

