



sanofi pasteur

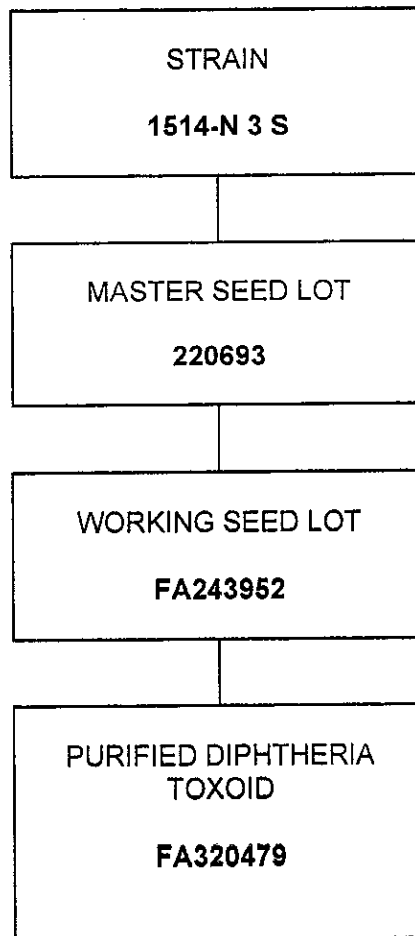
The vaccines division of sanofi-aventis Group

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° S4314 (clinical batch)

7/211

**



PRODUCTION FLOW SHEET

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 influenzae type b conjugate vaccine (adsorbed) lot n° S4314 (clinical batch)

8/211

 **

DIPHTHERIA STRAIN

Corynebacterium diphtheriae 1514-N-3S

STRAIN

Name	: Utrecht CN 2000 MSM III
Origin	: Rijks Instituut (RIV), Bilthoven Hollande
Received	: 01.12.69
Institut Mérieux number	: 1514-N-3S

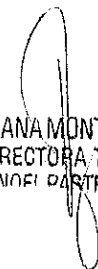

DIPHTHERIA MASTER SEED LOT

Lot n° 220693

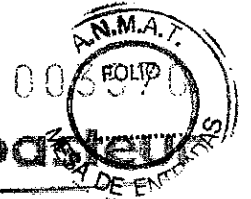
Strain number	: 1514-N-3S
Preparation date	: 22.06.93
Release date	: 21.04.94

CONTROLS

- Purity
 Identification
- Morphology
 - Growth characteristics
 - Biochemical characteristics

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**

DIPHTHERIA WORKING SEED LOT
Lot n° FA243952

Master seed Lot n° : 220693
Preparation date : 24.05.06
Release date : 15.12.06

CONTROLS

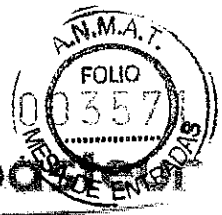
- Purity
- Identification
 - Morphology
 - Growth characteristics
 - Biochemical characteristics

The tests results show that working seed lot has the same characteristics as the master seed lot.


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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° S4314 (clinical batch)

10/211

**

DIPHTHERIA TOXOID
Lot n° FA312382

Strain : 1514-N-3S
Working seed-lot number : FA243952
Storage temperature : + 5°C ± 3°C
Approved storage period : 112 days

Single harvests :

Medium used : IMD (Pope and Linggood)
Date of reconstitution of seed lot ampoule(s) : 12.06.08
Date of inoculation : 18.06.08
Date of harvest : 20.06.08

CONTROLS

Identity test
Method : diphtheria flocculation
Date : 23.07.08
Result : positive

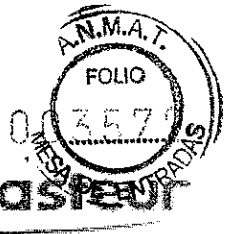
Bacterial purity
Method : Gram coloration
Date: 19.06.08
Result : conforms

Detoxification
Method : formaldehyde
Date of inactivation : 21.06.08

CONTROLS

Inactivation test (intradermic test) : conforms

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hepatitis B (rDNA), poliomyelitis (inactivated) and Haemophilus
influenzae type b conjugate vaccine (adsorbed) lot n° S4314 (clinical batch)

11/211

**

DIPHTHERIA TOXOID
Lot n° FA312383

Strain : 1514-N-3S
Working seed-lot number : **FA243952**
Storage temperature : + 5°C ± 3°C
Approved storage period : 112 days

Single harvests :

Medium used : IMD (Pope and Linggood)
Date of reconstitution of seed lot ampoule(s) : **15.06.08**
Date of inoculation : **21.06.08**
Date of harvest : **23.06.08**

CONTROLS

Identity test

Method : diphtheria flocculation
Date : **28.07.08**
Result : positive

Bacterial purity

Method : Gram coloration
Date: **22.06.08**
Result : conforms

Detoxification

Method : formaldehyde
Date of inactivation : **24.06.08**

CONTROLS

Inactivation test (intradermic test) : conforms


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Diphtheria, tetanus, pertussis (acellular, component),
hepatitis B (rDNA), poliomyelitis (inactivated) and Haemophilus
influenzae type b conjugate vaccine (adsorbed) lot n° S4314 (clinical batch)

12/211

**

DIPHTHERIA TOXOID
Lot n° FA312384

Strain	: 1514-N-3S
Working seed-lot number	: FA243952
Storage temperature	: + 5°C ± 3°C
Approved storage period	: 112 days

Single harvests :

Medium used	: IMD (Pope and Linggood)
Date of reconstitution of seed lot ampoule(s)	: 19.06.08
Date of inoculation	: 25.06.08
Date of harvest	: 27.06.08

CONTROLS

Identity test

Method : diphtheria flocculation
Date : 29.07.08
Result : positive

Bacterial purity

Method : Gram coloration
Date: 26.06.08
Result : conforms

Detoxification

Method : formaldehyde
Date of inactivation : 28.06.08

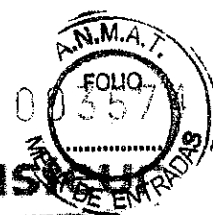
CONTROLS

Inactivation test (intradermic test) : conforms

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Product Quality and Disposition Department

Diphtheria, tetanus, pertussis (acellular, component),
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influenzae type b conjugate vaccine (adsorbed) lot n° S4314 (clinical batch) 13/211

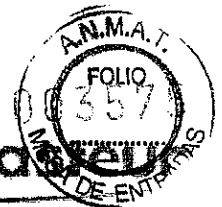
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PURIFIED DIPHTHERIA TOXOID
FA320479

TESTS	SPECIFICATIONS
PROTEIN NITROGEN CONTENT	For purity calculation
RESIDUAL FORMALDEHYDE CONTENT	For formulation
FLOCCULATING TITER	For purity calculation
ANTIGENIC PURITY	≥ 1500 Lf/mg of protein nitrogen
BACTERIAL AND FUNGAL STERILITY	No microbial growth
SPECIFIC TOXICITY	Negative
IRREVERSIBILITY OF TOXOID	Negative



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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° S4314 (clinical batch) 14/211

**

PURIFIED DIPHTHERIA TOXOID
Lot n° FA320479

Working seed Lot n° : FA243952

Diphtheria toxoid Lot number :	FA312382	FA312383	FA312384
Volume used (liters) :	490	390	450

Volume : 110.100 liters
Storage temperature : + 5°C ± 3°C
Date of manufacture : 08.09.08
Expiry date : 08 SEPTEMBER 2011
Approved storage period : 3 years

CONTROLS

Protein nitrogen content

Method : Kjeldahl after trichloroacetic acid precipitation
Date : 15.09.08
Result : 3.01 mg/ml

Residual formaldehyde content

Method : Nash
Date : 18.09.08
Result : 37.64 µg/ml

Flocculating titer

Method : Flocculation in comparison with in house
reference
Date : 12.09.08
Result : 5500 Lf/ml

Antigenic purity

Date : 27.10.08
Result : 1827 Lf/mg of protein nitrogen content

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Diphtheria, tetanus, pertussis (acellular, component),
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 influenzae type b conjugate vaccine (adsorbed) lot n° S4314 (clinical batch) 15/211

Bacterial and fungal sterility

Method	: Membrane filtration	
Media	: Thioglycollate	Soybean casein digest
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
Number of inoculated Steritest	: 1	1
Test on	: 15.09.08	
Test off	: 29.09.08	
Result	: No microbial growth - Conforms	


Specific toxicity


Method	: Vero cells
Reference standard toxin used	: FA142077-1 – 84 Lr/100 – 95 Lf/ml
Volume tested	: 200 µl of a 100 Lf/ml toxoid solution
Inoculum per well	: 50 µl
Test on	: 10.10.08
Test off	: 16.10.08
Result	: Negative - Conforms

Irreversibility of toxoid

Reference standard toxin used	: FA142077-1 – 84 Lr/100 – 95 Lf/ml	
Concentration of the toxoid solution	: 100 Lf/ml	100 Lf/ml
Incubation period	: 5°C ± 3°C	
Temperatures	: 37°C	
Date of beginning	: 19.09.08	
Date of end	: 31.10.08	

Method	: Vero cells	
Volume tested	: 200 µl	200 µl
Inoculum per well	: 50 µl	50 µl
Test on	: 05.12.08	
Test off	: 11.12.08	
Result	: Negative - Conforms	


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16/211

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- B - PURIFIED TETANUS TOXOID

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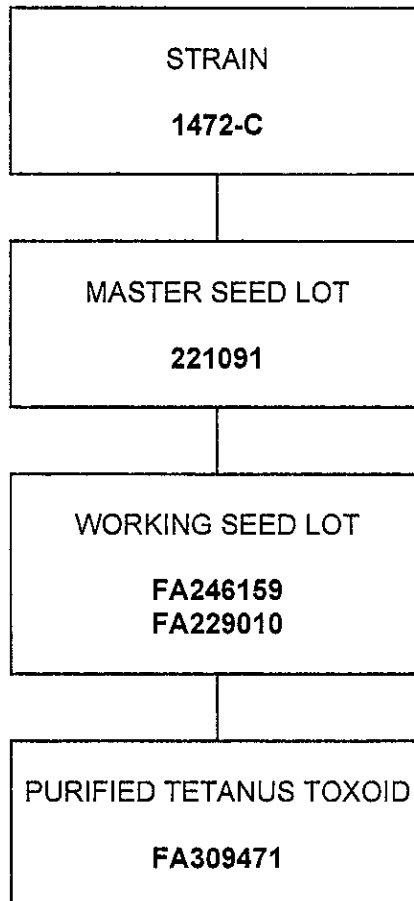
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hepatitis B (rDNA), poliomyelitis (inactivated) and Haemophilus
influenzae type b conjugate vaccine (adsorbed) lot n° S4314 (clinical batch)

17/211

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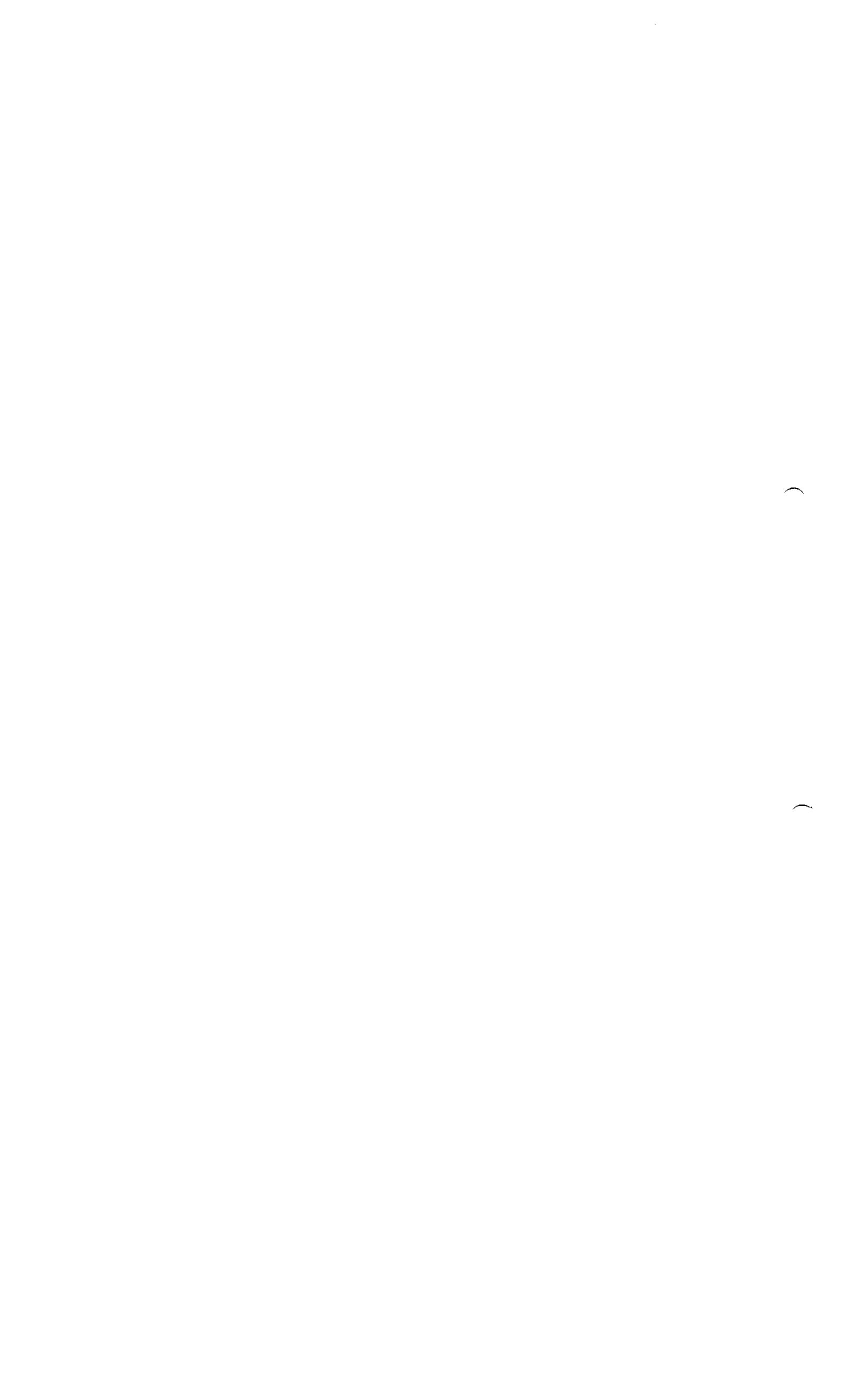


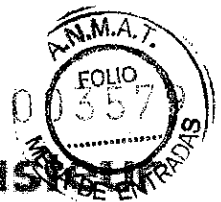
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352_CC5_SPL_AE.dot /19.09.11


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18/211

**

TETANUS STRAIN
Clostridium tetani 1472-C

STRAIN

Name : Harvard 49205
Origin : Rijks Institut (RIV), Bilthoven
Hollande (Y-IV-5 AV)
Received : 17.11.82
Institut Mérieux number : 1472-C

TETANUS MASTER SEED LOT
Lot n° 221091

Strain number : 1472-C
Preparation date : 22.10.91
Release date : 14.11.91

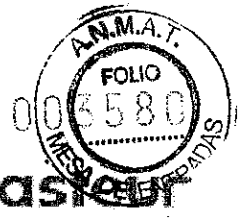
CONTROLS

- Purity
- Identification
 - Morphology
 - Growth characteristics
 - Biochemical characteristics

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19/211

**

TETANUS WORKING SEED LOT
Lot n° FA246159

Master seed Lot n° : 221091
Preparation date : 05.07.06
Release date : 22.11.06

CONTROLS

- Purity
- Identification
 - Morphology
 - Growth characteristics
 - Biochemical characteristics

The tests results show that working seed lot has the same characteristics as the master seed lot.


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Diphtheria, tetanus, pertussis (acellular, component),
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20/211

**

TETANUS WORKING SEED LOT
Lot n° FA229010

Master seed Lot n° : 221091
Preparation date : 20.12.05
Release date : 19.01.09

CONTROLS

- Purity
- Identification
 - Morphology
 - Growth characteristics
 - Biochemical characteristics

The tests results show that working seed lot has the same characteristics as the master seed lot.


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