

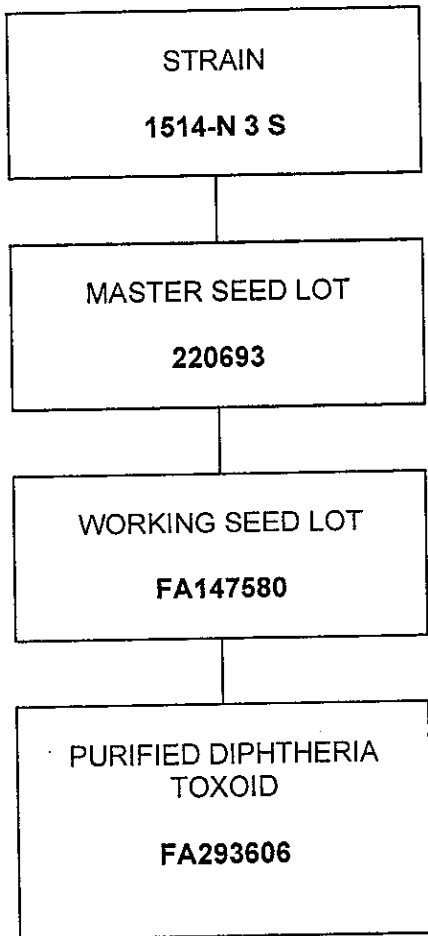
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The vaccines division of sanofi-aventis Group

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)

7/180



PRODUCTION FLOW SHEET

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 SANOFI PASTEUR S.A.

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 CHRISTIAN DOMÍNGUEZ
 GERENTE
 SANOFI PASTEUR S.A.



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8/180

DIPHTHERIA STRAIN

Corynebacterium diphtheriae 1514-N-3S

STRAIN

Name	: Utrecht CN 2000 MSM III
Origin	: Rijks Institut (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	: 06.06.95

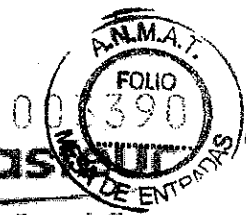
CONTROLS

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


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DIPHTHERIA WORKING SEED LOT
Lot n°FA147580

Master seed Lot n° : 220693
Preparation date : 09.04.03
Release date : 11.07.03

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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influenzae type b conjugate vaccine (adsorbed) lot n° S4313 (clinical batch) 10/180

DIPHTHERIA TOXOID
Lot n°FA285546

Strain : 1514-N-3S
Working seed-lot number : FA147580
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) : 06.09.07
Date of inoculation : 12.09.07
Date of harvest : 14.09.07

CONTROLS

Identity test
Method : diphtheria flocculation
Date : 06.11.07
Result : positive

Bacterial purity
Method : Gram coloration
Date: 13.09.07
Result : conforms

Detoxification
Method : formaldehyde
Date of inactivation : 15.09.07

CONTROLS

Inactivation test (intradermic test) : conforms

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11/180

DIPHTHERIA TOXOID
Lot n°FA285655

Strain : 1514-N-3S
Working seed-lot number : FA147580
Storage temperature : + 5°C ± 3°C
Approved storage period : 112 days

Single harvests :

Medium used : IMD (Pope and Lingood)
Date of reconstitution of seed lot ampoule(s) : 09.09.07
Date of inoculation : 15.09.07
Date of harvest : 17.09.07

CONTROLS

Identity test
Method : diphtheria flocculation
Date : 06.11.07
Result : positive

Bacterial purity
Method : Gram coloration
Date: 16.09.07
Result : conforms

Detoxification
Method : formaldehyde
Date of inactivation : 18.09.07

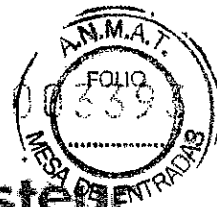
CONTROLS

Inactivation test (intradermic test) : conforms

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12/180

DIPHTHERIA TOXOID
Lot n°FA285656

Strain	: 1514-N-3S
Working seed-lot number	: FA147580
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)	: 13.09.07
Date of inoculation	: 19.09.07
Date of harvest	: 21.09.07

CONTROLS

Identity test

Method : diphtheria flocculation
Date : **16.11.07**
Result : positive

Bacterial purity



Method : Gram coloration
Date: **20.09.07**
Result : conforms

Detoxification

Method : formaldehyde
Date of inactivation : **22.09.07**

CONTROLS

Inactivation test (intradermic test) : conforms

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13/180

PURIFIED DIPHTHERIA TOXOID
FA293606

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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PURIFIED DIPHTHERIA TOXOID
Lot n° FA293606

Working seed Lot n° : FA147580

Diphtheria toxoid Lot number :	FA285546	FA285655	FA285656
Volume used (liters) :	410	460	440

Volume : 99.3 liters
 Storage temperature : + 5°C ± 3°C
 Date of manufacture : 19.11.07
 Expiry date : 19 NOVEMBER 2010
 Approved storage period : 3 years

CONTROLS

Protein nitrogen content

Method : Kjeldahl after trichloroacetic acid precipitation
 Date : 11.12.07
 Result : 3.32 mg/ml

Residual formaldehyde content

Method : Nash
 Date : 05.12.07
 Result : 32.51 µg/ml

Flocculating titer

Method : Flocculation in comparison with in house
reference
 Date : 03.12.07
 Result : 5500 Lf/ml

Antigenic purity

Date : 19.12.07
 Result : 1657 Lf/mg of protein nitrogen

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Diphtheria, tetanus, pertussis (acellular, component),
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 influenzae type b conjugate vaccine (adsorbed) lot n° S4313 (clinical batch) 15/180

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	: 27.11.07	
Test off	: 11.12.07	
Result	: No microbial growth - Conforms	



Specific toxicity

Method	: Vero cells
Reference standard toxin used	: FA142077-1
Volume tested	: 200 µl of a 100 Lf/ml toxoid solution
Inoculum per well	: 50 µl
Test on	: 07.12.07
Test off	: 13.12.07
Result	: Negative - Conforms

Irreversibility of toxoid

Reference standard toxin used	: FA142077-1	
Concentration of the toxoid solution	: 100 Lf/ml	100 Lf/ml
Incubation period	: 5°C ± 3°C	
Temperatures	: 37°C	
Date of beginning	: 07.12.07	
Date of end	: 18.01.08	

<i>Method</i>	: Vero cells	
Volume tested	: 200 µl	200 µl
Inoculum per well	: 50 µl	50 µl
Test on	: 25.01.08	
Test off	: 31.01.08	
Result	: Negative - Conforms	



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16/180

- B - PURIFIED TETANUS TOXOID


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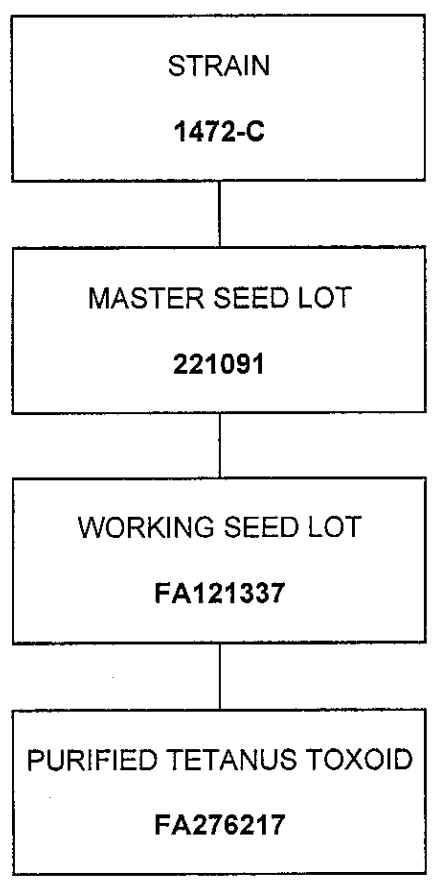


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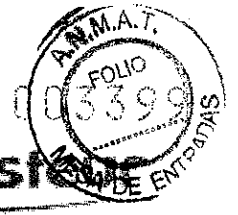


PRODUCTION FLOW SHEET

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18/180

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 TOXOID
Master seed 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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19/180

TETANUS WORKING SEED LOT
Lot n°FA121337

Master seed Lot n° : 221091
Preparation date : 24.07.02
Release date : 29.10.02

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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