



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)

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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 : FA331636

Date of manufacture : 18.11.08
Storage temperature : +5°C ± 3°C
Expiry date : 18 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	FA291505	55.850
	FA304026	29.834
Monovalent type 2	FA293397	28.470
Monovalent type 3	FA300586	68.352
	FA288122	19.068
199 Medium	FA322175	98.426
APPROXIMATE TOTAL VOLUME		298 700

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CONTROLS :

pH measurement

Method : Glass electrode
Date : 28.11.08
Result : 7.15 - **Conforms**

Residual formaldehyde content

Method : Spectrophotometry
Date : 25.11.08
Result : 52.97 µg/ml - **Conforms**

Bovine serum albumin content


Method : ELISA
Date : 25.11.08
Result : <3.9 ng/ml - **Conforms**


Bacterial endotoxins content

Method : LAL
Date : 25.11.08
Result : <0.50 IU/ml - **Conforms**

Bacterial and fungal sterility

Method used	:	Membrane filtration	
Media	:	Thioglycollate medium	Soybean Casein Digest medium
Temperatures	:	30-35° 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	:	20.11.08	
Test off	:	04.12.08	
Result	:	Conforms	


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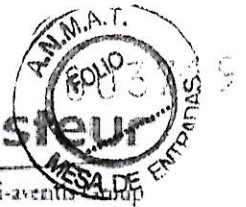
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- F - HAEMOPHILUS type b CONJUGATE


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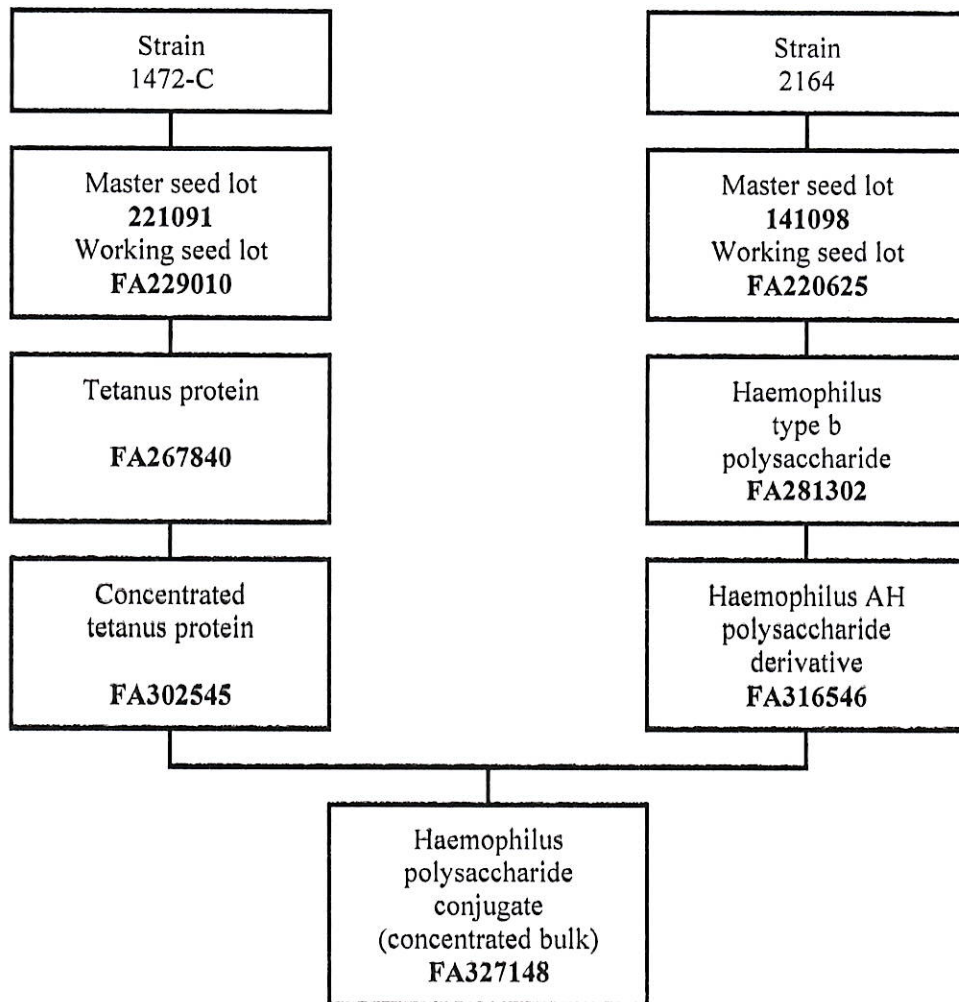
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PRODUCTION FLOW SHEET



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HAEMOPHILUS INFLUENZAE
 Strain : Haemophilus Influenzae 2164

STRAIN

Name	: Haemophilus influenzae type b – strain 1482
Origin	: Dr John ROBBINS (FDA) Bethesda – Maryland 20014
Received	: 12.12.75
Institut Mérieux number	: IM 2164

HAEMOPHILUS INFLUENZAE
 Master seed lot n° 141098

Strain number	: IM 2164
Preparation date	: 14.10.98
Release date	: 11.09.01

CONTROLS

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

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HAEMOPHILUS INFLUENZAE
 Working seed lot n° FA220625

Master seed Lot n°	: 141098
Preparation date	: 15.09.05
Release date	: 22.11.05

CONTROLS

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

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

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TETANUS TOXOID
Strain : Clostridium tetani 1472-C

STRAIN

Name : Harvard 49205 strain identified by the n°Y-IV-5A
Origin : Rijks Instituut (RIV), Bilthoven
Netherlands
Received : 17.11.82
Institut Mérieux number : IM 1472-C

TETANUS TOXOID
Master seed lot n° 221091

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

CONTROLS

- Purity
Identification
- Morphology
 - Growth characteristics
 - Biochemical characteristics

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TETANUS TOXOID
Working seed 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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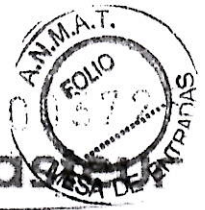
CONCENTRATED TETANUS PROTEIN

TESTS	SPECIFICATIONS
TETANUS PROTEIN	
PROTEIN NITROGEN CONTENT (PN)	For calculation
TOTAL NITROGEN CONTENT (TN)	For calculation
PN/TN RATIO	≥ 0.8
OD280/OD260 RATIO	≥ 1.3
FLOCCULATING TITRE	For calculation
ANTIGENIC PURITY	> 1500 Lf/mg of protein nitrogen
MOLECULAR SIZE DISTRIBUTION	≥ 50 % of monomers
BACTERIAL AND FUNGAL STERILITY	No microbial growth
CONCENTRATED TETANUS PROTEIN	
PROTEIN NITROGEN CONTENT	For calculation
OD280/OD260 RATIO	≥ 1.3
PHOSPHORUS CONTENT	< 1.5 µg/mg of protein
RESIDUAL FORMALDEHYDE CONTENT	< 10 µg/mg of protein
FLOCCULATING TITRE	For calculation
ANTIGENIC PURITY	> 1500 Lf/mg of protein nitrogen
MOLECULAR SIZE DISTRIBUTION	≥ 50 % of monomers
BACTERIAL AND FUNGAL STERILITY	No microbial growth
SPECIFIC TOXICITY	Conforms
IRREVERSIBILITY OF TETANUS TOXOID	Conforms
PYROGENS	Conforms

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CONCENTRATED TETANUS PROTEIN
lot number : FA302545

Date of manufacture : 19.03.2008
Storage temperature : + 5 °C ± 3°C
Expiry date : 19 MARCH 2009
Volume : 3.572 liters

TETANUS PROTEIN CONTROLS :

Protein nitrogen content (PN)

Method : Kjeldahl after trichloroacetic acid precipitation
Date : 12.04.07
Result : 0.110 mg/ml

Total nitrogen content (TN)

Method : Kjeldahl
Date : 12.04.07
Result : 0.122 mg/ml

PN/TN ratio : 0.90 - Conforms

OD280/OD260 ratio : 1.88 - Conforms

Flocculating titre

Method : Flocculation determined from in-house reference
Date : 20.04.07
Result : 270 Lf/ml

Antigenic purity

Result : 2455 Lf/mg of protein nitrogen - Conforms

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Molecular size distribution

Method : size exclusion Chromatography
Date : 17.04.07
Result : 66.80 % of monomers – **Conforms**

Bacterial and fungal sterility

Method	:	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	:	16.04.07	
Test off	:	30.04.07	
Result	:	No microbial growth - Conforms	

CONCENTRATED TETANUS PROTEIN CONTROLS :

Protein nitrogen content

Method : Kjeldahl after trichloroacetic acid precipitation
Date : 31.03.08
Result : 5.25 mg/ml

OD280/OD260 ratio : 1.89 - Conforms

Phosphorus content

Method : Chen
Date : 09.04.08
Result : <0.04 µg/mg of protein - **Conforms**

Residual formaldehyde content

Method : Nash
Date : 26.03.08
Result : 0.48 µg/mg of protein - **Conforms**

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Flocculating titre

Method : Flocculation determined from in-house reference
 Date : 25.03.08
 Result : 12000 Lf/ml

Antigenic purity

Result : 2286 Lf/mg of protein nitrogen - **Conforms**

Molecular size distribution

Method : size exclusion Chromatography
 Date : 10.04.08
 Result : 65.10 % of monomers – **Conforms**

Bacterial and fungal sterility

Method	:	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	:	20.03.08	
Test off	:	03.04.08	
Result	:	No microbial growth - Conforms	

Specific toxicity test

Animals : Guinea-pigs
 Number of animals : 5
 Lf of toxoid injected per animal : 2000
 Route : Subcutaneous
 Test on : 03.04.08
 Test off : 24.04.08
 Result : **Conforms**




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