

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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Composition of single human dose \* :

Purified diphtheria toxoid	: 30 Lf (≥ 20 IU †)
Purified tetanus toxoid	: 10 Lf (≥ 40 IU †)
<i>Bordetella pertussis</i> antigens	
Adsorbed purified pertussis toxoid	: 25 µg
Adsorbed purified filamentous haemagglutinin	: 25 µg
Inactivated poliomyelitis virus (produced on Vero cells)	
Type 1 (Mahoney)	: 40 DU §
Type 2 (MEF-1)	: 8 DU §
Type 3 (Saukett)	: 32 DU §
Hepatitis B surface antigen **	: 10 µg
Haemophilus influenzae type b polysaccharide (polyribosylribitol phosphate)	: 12 µg
Conjugated to Tetanus protein (PRP-T)	: 18-30 µg
Aluminium hydroxide, hydrated, for adsorption	: 0.6 mg Al <sup>3+</sup>
Buffer solution :	
Disodium hydrogen phosphate	: 1.528 mg
Potassium dihydrogen phosphate	: 1.552 mg
Essential amino acids ‡	: 1.115 mg
Trometamol	: 0.1515 mg
Saccharose	: 10.625 mg
Water for injections	: up to 0.5 ml

\* NaOH, acetic acid, or HCl can be used for pH adjustment. these components are only present in trace amount.

† As lower confidence limit (p = 0.95)

§ Or equivalent antigenic quantity determined by suitable immunochemical method

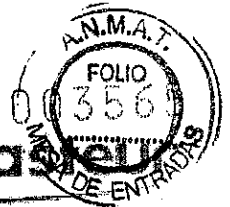
\*\* Produced in yeast *Hansenula polymorpha* cells by recombinant DNA technology

‡ Essentials amino acids including L-phenylalanine

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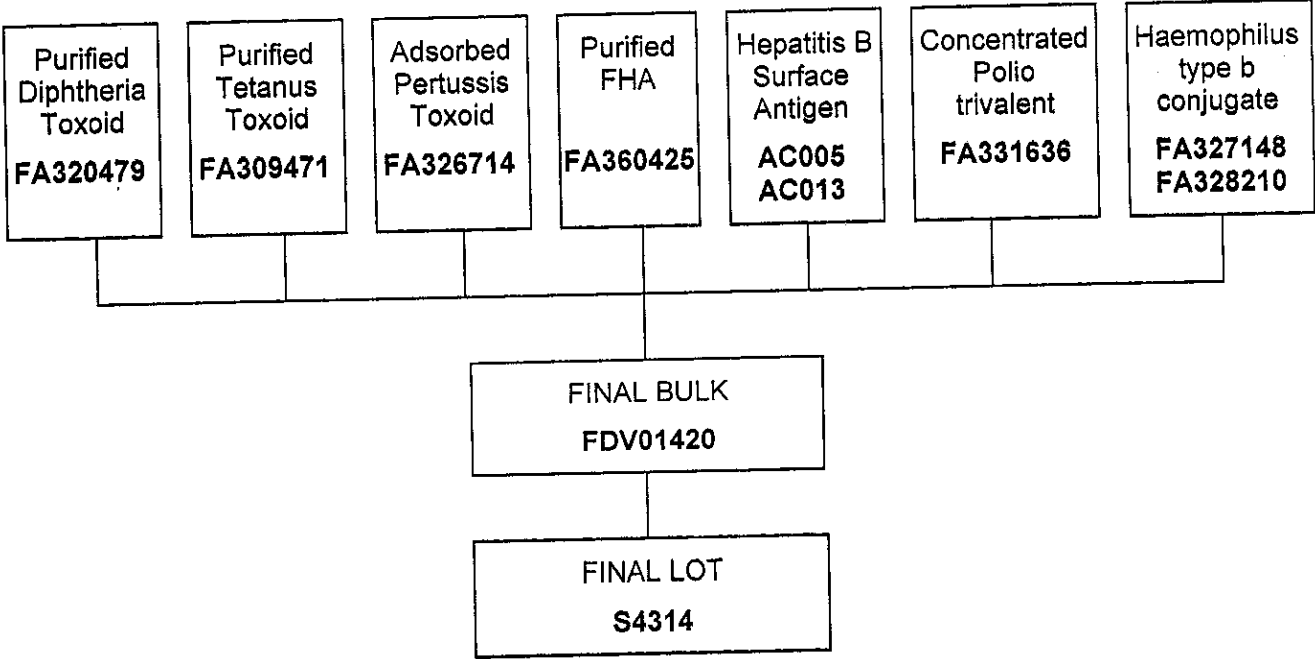
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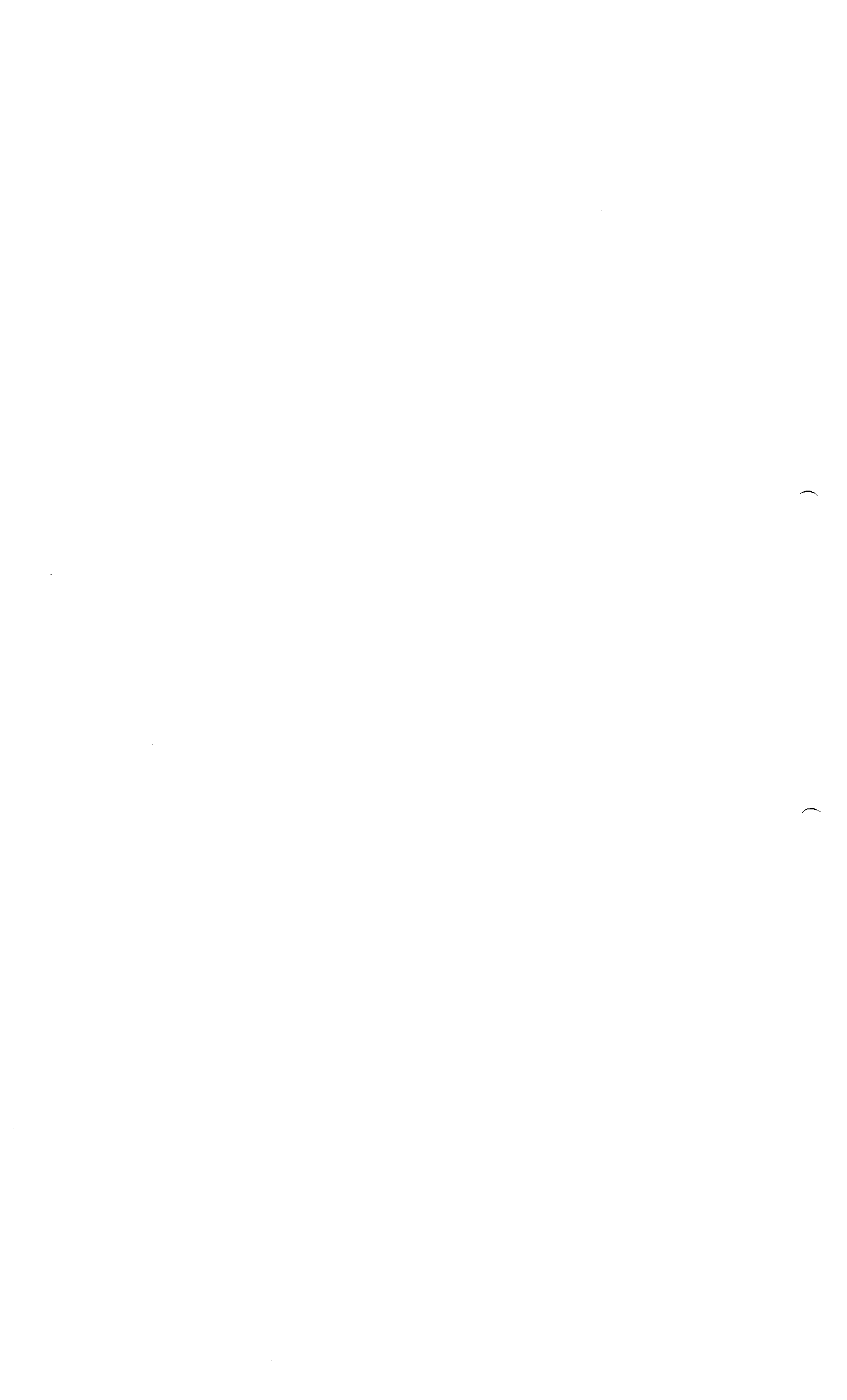
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**PART 1**  
**ACTIVE INGREDIENTS**

- A - PURIFIED DIPHTHERIA TOXOID**
- B - PURIFIED TETANUS TOXOID**
- C - 2 COMPONENT ACELLULAR PERTUSSIS**
- D - HEPATITIS B**
- E - INACTIVATED POLIOMYELITIS TRIVALENT**
- F - HAEMOPHILUS type b CONJUGATE**

  
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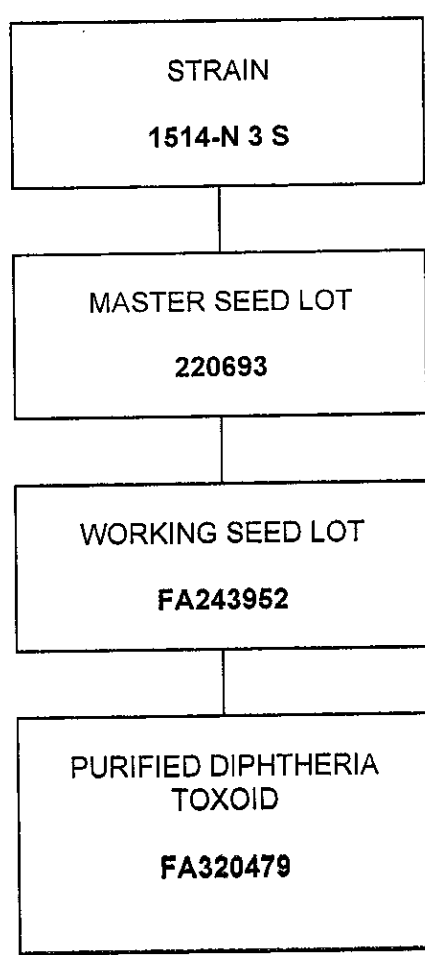
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**DIPHTHERIA STRAIN**  
  
**Corynebacterium diphtheriae 1514-N-3S**

**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**

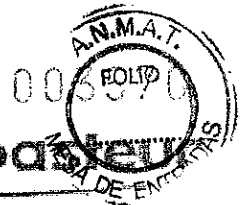
Strain number	: 1514-N-3S
Preparation date	: <b>22.06.93</b>
Release date	: <b>21.04.94</b>

**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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**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**

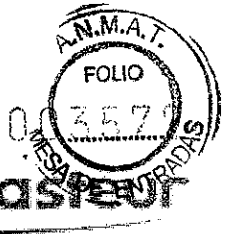
**CONTROLS**

Inactivation test (intradermic test) : conforms

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**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

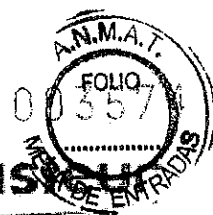
  
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PURIFIED DIPHTHERIA TOXOID  
FA320479

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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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**

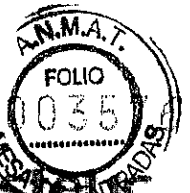
Method : Flocculation in comparison with in house  
reference  
 Date : 12.09.08  
 Result : 5500 Lf/ml

**Antigenic purity**

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

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**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	:		
Temperatures	:	5°C ± 3°C	37°C
Date of beginning	:	19.09.08	
Date of end	:	31.10.08	

<i>Method</i>	:	<i>Vero cells</i>	
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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**- B - PURIFIED TETANUS TOXOID**

  
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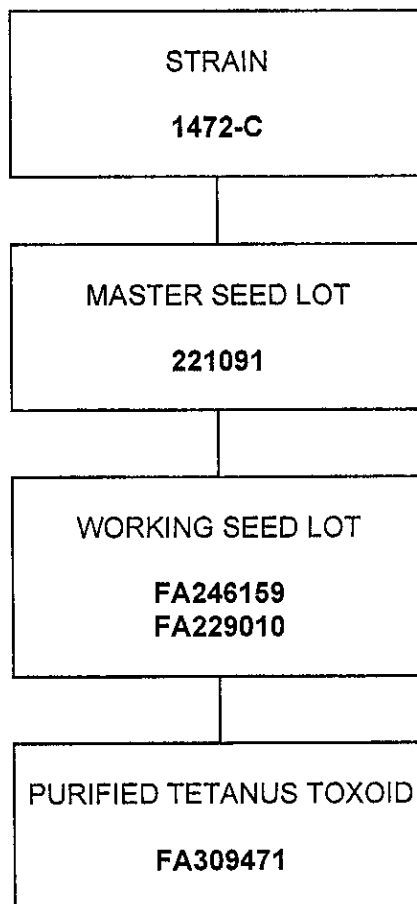
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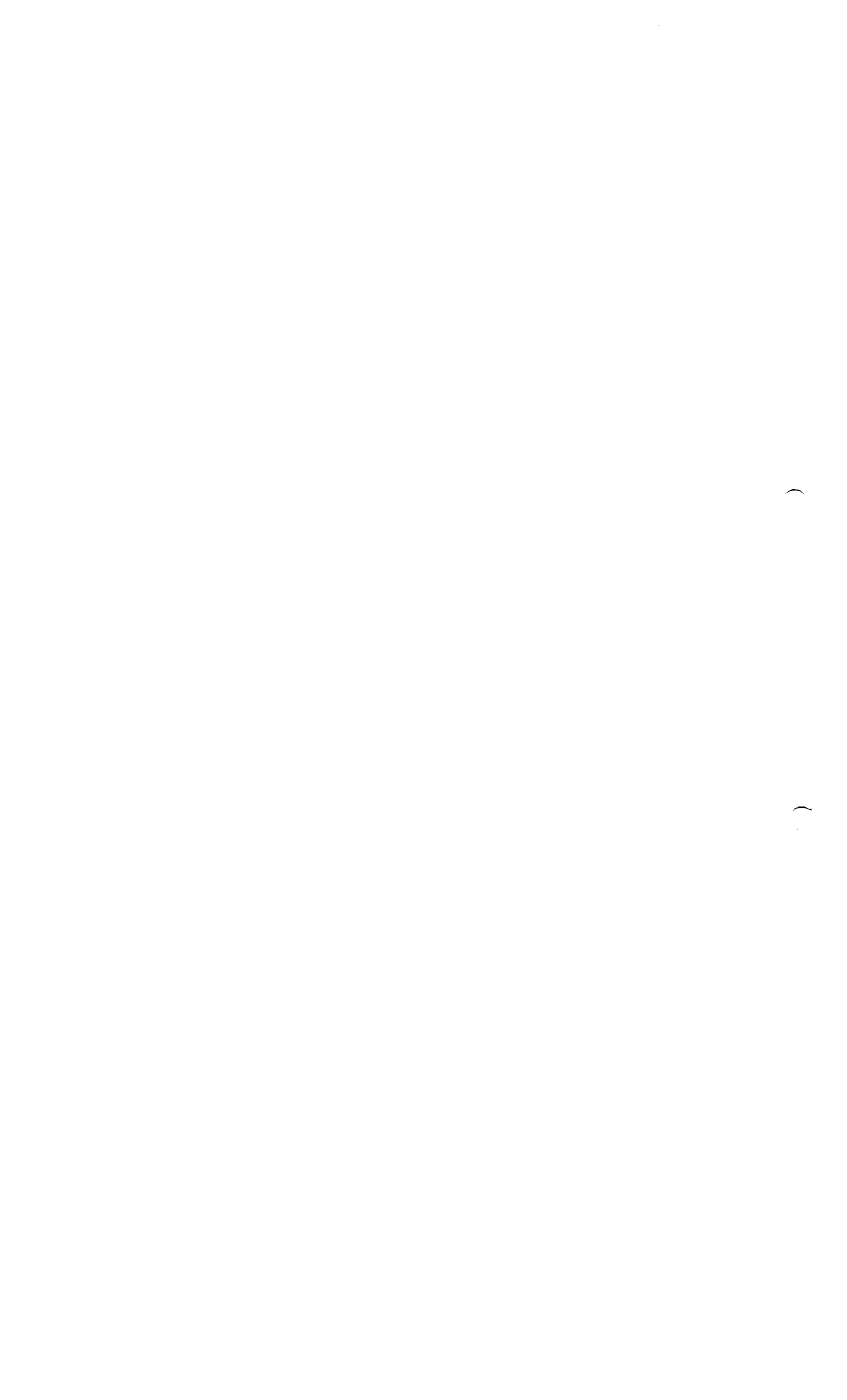
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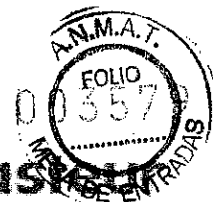


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**TETANUS STRAIN**  
**Clostridium tetani 1472-C**

**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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**TETANUS WORKING SEED LOT**  
**Lot n° FA246159**


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

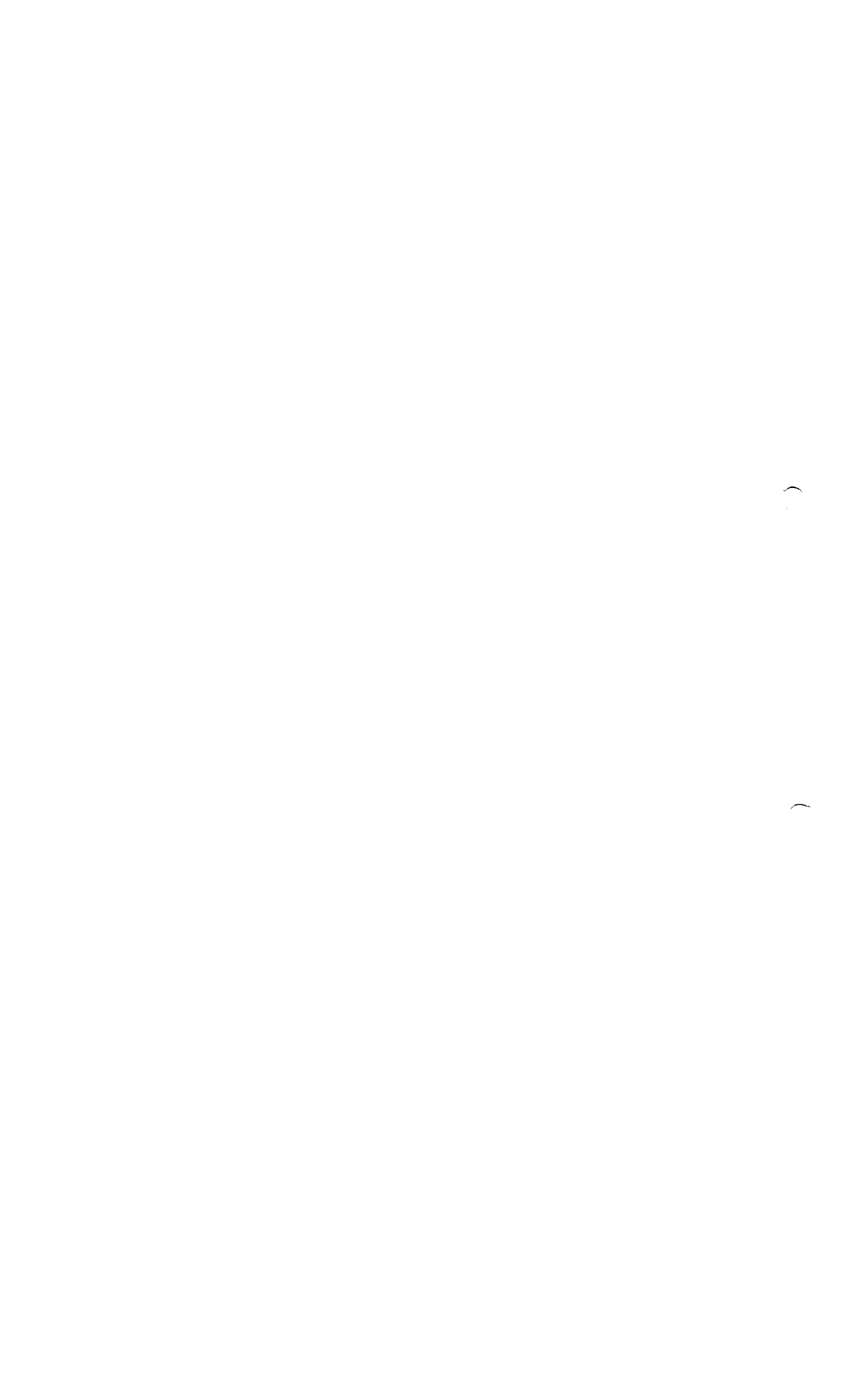
**CONTROLS**

- 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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**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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