

Lot ----
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Plasmid structural stability (Specification: Conforms to standard)

Method Plasmid structural stability test
Date of test -----
Result -----

Plasmid sequence (Specification: Conforms to standard)

Method Sequencing of coding region of plasmid
Date of test -----
Result -----

Plasmid copy number (Specification: Report result)

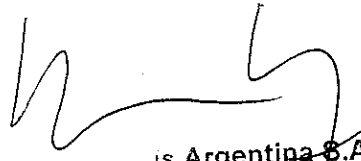
Method Plasmid copy number test
Date of test -----
Result ---- copies/bacterium

Bacteriophages (Specification: Conforms to standard)

Method Inoculation on plates and observation
Date of test -----
Result -----

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Production details of working seed

Name and address of manufacturer Novartis Vaccines and Diagnostics Srl
Bellaria - Rosia, 53018 Sovicille - Siena (Italy)

Lot of master seed used in manufacture -----

Working seed lot -----

Date of manufacture of working seed -----

Added preservatives in working seed None

Storage conditions of working seed - 80 ± 10°C

Tests on working seed

Purity test (Specification: Absence of contaminants)

Method Inoculation on plates and microscopic observation
Date of test -----
Result -----

Identity tests (Specification: Positive)

Method API identification
Date of test -----
Result -----

Method Western blot
Date of test -----
Result -----

Vitality test (Specification: ≥ 10⁸ CFU/mL)

Method Inoculation on plates and colony count
Date of test -----
Result --- x 10⁻⁻⁻ CFU/mL

Plasmid copy number (Specification: Report result)

Method Plasmid copy number test
Date of test -----
Result ----- copy/bacterium

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MEN B RECOMBINANT PROTEIN 287 - 953 CONCENTRATED BULK LOT -----

Production details of Men B recombinant protein 287 - 953 concentrated bulk

Name and address of manufacturer	Sandoz GmbH Biochemiestrasse, 10 – A-6250 Kundl (Austria)
Lot of working seed used in manufacture	-----
Date of thawing of working seed for manufacture	-----
Date of inoculum	-----
Culture media used in fermentation	Solution of PTK yeast extract, yeast extract, sodium chloride, PPG, magnesium chloride hexahydrate, calcium chloride, and glycerol, supplemented with IPTG (induction)
Temperature of incubation	34 – 38 °C
Date of harvest	-----
Volume of harvest	----- Kg
Purification procedure	Centrifugation, chromatography and ultrafiltration
Date of manufacture	-----
Volume of Men B recombinant protein 287 - 953 concentrated bulk	----- mL
Expiry date	-----
Approved storage period	36 months
Storage conditions of Men B recombinant protein 287 - 953 concentrated bulk	≤ - 15°C (protected from light)

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Test on Men B recombinant protein 287 - 953 concentrated bulk

Identity test (Specification: Positive)

Method Western blot
Date of test -----
Result -----

Purity test (Specification: $\geq 90\%$)

Method SDS - PAGE
Date of test -----
Result ----- %

Total protein content (Specification: 500 - 1100 mcg/mL)

Method BCA
Date of test -----
Result ----- mcg/mL

Endotoxin content (Specification: ≤ 0.16 IU/mcg protein)

Method LAL test
Date of test -----
Result ----- IU/ mcg protein

Purity test (Specification: $\geq 70\%$)

Method SE-HPLC
Date of test -----
Result ----- %

Osmolarity (Specification: 600 - 750 mOsm/Kg) (*)

Method Eur. Ph./USP
Date of test -----
Result ----- mOsm/Kg

Residual *E. coli* HCP (Specification: ≤ 50 ppm) (*)

Method Ratio ELISA *E. Coli*/ protein
Date of test -----
Result ----- ppm

(*) Test performed at Novartis Vaccines and Diagnostics - Italy

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Conductivity (Specification: 11000 - 14500 µS/cm)

Method Potentiometric
Date of test -----
Result ----- µS/cm

pH (Specification: 6.5 -7.5)

Method Potentiometric
Date of test -----
Result -----

Bioburden (Specification: ≤ 10 CFU/100 mL)

Method Eur. Ph./USP, membrane filtration
Media TSA
Volume tested ----- mL
Date of test Record date beginning - date end
Result ----- CFU/100 mL

Ox - red ratio (Specification: Report result)

Method RP-HPLC
Date of test -----
Result ----- %

Unspecified Impurities (Specification: ≤ 9%)

Method SE-HPLC
Date of test -----
Result ----- %

CERTIFICATION

I herewith certify that Men B Recombinant Protein 287 - 953 Concentrated Bulk Lot No. ----- was manufactured and tested according to the procedures approved by competent authorities and complies with the quality requirements. This includes that, for any material derived from ruminants (bovine, ovine, caprine) used in the manufacture and/or formulation of the batch of product specified above, all measures have been taken to demonstrate compliance with Directive 2001/83/EC and amending Directives 2003/63/EC and 2004/27/EC.

In addition the OMCL performing OCABR has been notified of all relevant approved variations that have an impact on product specifications or on data supplied in section 3 of this protocol as described in the EU administrative procedure for OCABR.

Dr. -----
Quality Operations / Qualified Person

Novartis Argentina S.A.
Dr. Lucio Jeronimo
Director Técnico
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Date

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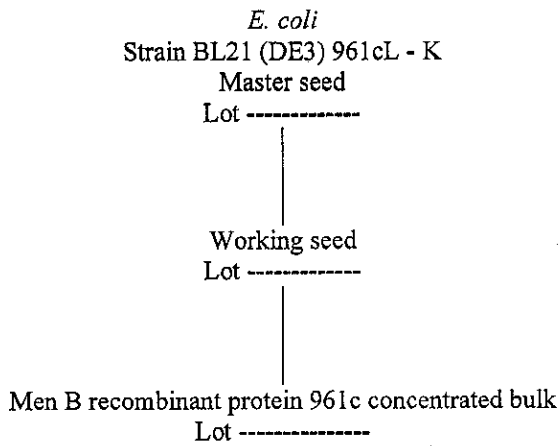
**SUMMARY PROTOCOL FOR PRODUCTION AND TESTING
OF RECOMBINANT MENINGOCOCCAL GROUP B PROTEIN 961c
CONCENTRATED BULK**

LOT -----

Summary

	Page
- Production Plan	----
- <i>E. coli</i> starting material	----
- Men B recombinant protein 961c concentrated bulk	Lot ----- ----

PRODUCTION PLAN



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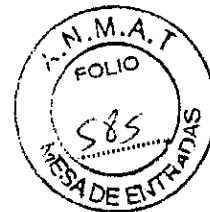
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E. COLI STARTING MATERIAL

Production details of master seed

Name and address of manufacturer	Novartis Vaccines and Diagnostics Srl Bellaria - Rosia, 53018 Sovicille - Siena (Italy)
<i>E. coli</i> strain	BL21 (DE3) 961cL - K
Master seed lot	-----
Date of manufacture of master seed	-----
Added preservatives in master seed	None
Storage conditions of master seed	Liquid nitrogen

Tests on master seed

Purity test (Specification: Absence of contaminants)

Method	Inoculation on plates and microscopic observation
Date of test	-----
Result	-----

Identity tests (Specification: Positive)

Method	API identification
Date of test	-----
Result	-----

Method	Western blot
Date of test	-----
Result	-----

Vitality test (Specification: $\geq 10^8$ CFU/mL)

Method	Inoculation on plates and colony count
Date of test	-----
Result	--- x 10 ⁻⁻⁻ CFU/mL

Plasmid retention (Specification: ≤ 10 % cells without plasmid)

Method	Plasmid retention test
Date of test	-----
Result	----- % cells without plasmid

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Production details of working seed

Name and address of manufacturer Novartis Vaccines and Diagnostics Srl
Bellaria - Rosia, 53018 Sovicille - Siena (Italy)

Lot of master seed used in manufacture -----

Working seed lot -----

Date of manufacture of working seed -----

Added preservatives in working seed None

Storage conditions of working seed - 80 ± 10°C

Tests on working seed

Purity test (Specification: Absence of contaminants)

Method Inoculation on plates and microscopic observation
Date of test -----
Result -----

Identity tests (Specification: Positive)

Method API identification
Date of test -----
Result -----

Method Western blot
Date of test -----
Result -----

Vitality test (Specification: ≥ 10⁸ CFU/mL)

Method Inoculation on plates and colony count
Date of test -----
Result --- x 10⁻⁻⁻ CFU/mL

Plasmid copy number (Specification: Report result)

Method Plasmid copy number test
Date of test -----
Result ----- copy/bacterium

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MEN B RECOMBINANT PROTEIN 961c CONCENTRATED BULK LOT -----


Production details of Men B recombinant protein 961c concentrated bulk

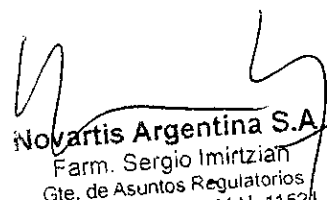
Name and address of manufacturer	Sandoz GmbH Biochemiestrasse, 10 – A-6250 Kundl (Austria)
Lot of working seed used in manufacture	-----
Date of thawing of working seed for manufacture	-----
Date of inoculum	-----
Culture media used in fermentation	Solution of PTK yeast extract, yeast extract, sodium chloride, PPG, Magnesium chloride hexahydrate, calcium chloride and glycerol, supplemented with IPTG (induction)
Temperature of incubation	34 – 38 °C
Date of harvest	-----
Volume of harvest	----- Kg
Purification procedure	Centrifugation, chromatography and ultrafiltration
Date of manufacture	-----
Volume of Men B recombinant protein 961c concentrated bulk	----- mL
Expiry date	-----
Approved storage period	36 months
Storage conditions of Men B recombinant protein 961c concentrated bulk	≤ - 15°C (protected from light)

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Prot. ----/-

Test on Men B recombinant protein 961c concentrated bulk

Identity test (Specification: Positive)

Method Western blot
Date of test -----
Result -----

Purity and integrity test (Specification: Purity \geq 90 %; Integrity \geq 70 %)

Method SDS - PAGE
Date of test -----
Result Purity: ----- %
Integrity: ----- %

Total protein content (Specification: 1000 - 3000 mcg/mL)

Method BCA
Date of test -----
Result ----- mcg/mL

Endotoxin content (Specification: \leq 0.16 IU/mcg protein)

Method LAL test
Date of test -----
Result ----- IU/ mcg protein

Purity test (Specification: \geq 89 %)

Method SE-HPLC
Date of test -----
Result ----- %

Residual *E. coli* HCP (Specification: \leq 50 ppm) (*)

Method Ratio ELISA *E. Coli* protein
Date of test -----
Result ----- ppm

Osmolarity (Specification: 240 – 360 mOsm/Kg) (*)

Method Eur. Ph./USP
Date of test -----
Result ----- mOsm/Kg

(*) Test performed at Novartis Vaccines and Diagnostics - Italy

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Conductivity (Specification: 15000 - 17300 μ S/cm)

Method Potentiometric
Date of test -----
Result ----- μ S/cm

pH (Specification: 6.5 -7.5)

Method Potentiometric
Date of test -----
Result -----

Bioburden (Specification: \leq 10 CFU/100 mL) (*)

Method Eur. Ph./USP, membrane filtration
Media TSA
Volume tested ----- mL
Date of test Record date beginning - date end
Result ----- CFU/100 mL

CERTIFICATION

I herewith certify that Men B Recombinant Protein 961c Concentrated Bulk Lot No. ----- was manufactured and tested according to the procedures approved by competent authorities and complies with the quality requirements. This includes that, for any material derived from ruminants (bovine, ovine, caprine) used in the manufacture and/or formulation of the batch of product specified above, all measures have been taken to demonstrate compliance with Directive 2001/83/EC and amending Directives 2003/63/EC and 2004/27/EC.

In addition the OMCL performing OCABR has been notified of all relevant approved variations that have an impact on product specifications or on data supplied in section 3 of this protocol as described in the EU administrative procedure for OCABR.

Dr. -----
Quality Operations / Qualified Person

Date

(*) Specification effective from August 09, 2013. The specification for any batch tested prior to August 09, 2013 is to be considered as \leq 17 CFU/100 mL.

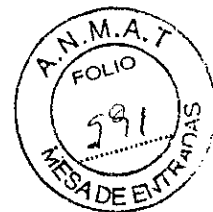
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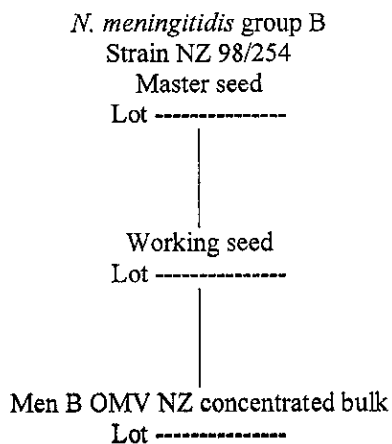
**SUMMARY PROTOCOL FOR PRODUCTION AND TESTING
OF MENINGOCOCCAL GROUP B OMV NZ
PURIFIED CONCENTRATED BULK**

LOT -----

Summary

	Page
- Production Plan	----
- <i>N. meningitidis</i> group B starting material	----
- Men B OMV NZ concentrated bulk	Lot ----- ----

PRODUCTION PLAN



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