Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
2nd WHO International Standard for Meningococcal Capsular Group C Polysaccharide
NIBSC code: 20/314
Instructions for use
(Version 1.0, Dated 26/05/2023)

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1. INTENDED USE

The freeze-dried preparation of Neisseria meningitidis capsular group C (MenC) polysaccharide (PS), provided by the Serum Institute of India, Pune, India, was prepared in ampoules in 2021 at the Centre for Biological Reference Materials (CBRM) at the South Mimms laboratories of the Medicines and Healthcare products Regulatory Agency (MHRA). MenC content (mg per ampoule) was determined by 12 laboratories performing quantitative nuclear magnetic resonance (qNMR) spectroscopy. Other assays (including the resorcinol assay and high performance anionic exchange chromatography with pulsed amperometric detection (HPAEC-PAD) were also performed for the collaborative study to evaluate polysaccharide content and suitability for use as a standard for quantification of MenC in materials relevant to vaccine production (purified and conjugated PS). The material is suitable for use in the quantitation of MenC content by other assays, although users should verify its suitability and determine the uncertainly of measurement in their specific assay. The MHRA, South Mimms (NIBSC) UK is the custodian and distributor of this material.

2. CAUTION

This preparation is not for administration to humans or animals in the human food chain.

The material is not of human or bovine origin. As with all materials of biological origin, this preparation should be regarded as potentially hazardous to health. It should be used and discarded according to your own laboratory's safety procedures. Such safety procedures should include the wearing of protective gloves and avoiding the generation of aerosols. Care should be exercised in opening ampoules or vials, to avoid cuts.

3. UNITAGE

The 2nd WHO International Standard for Meningococcal Capsular Group C Polysaccharide, 20/314, has a content of 0.965 ± 0.024 mg MenC PS per ampoule (expanded uncertainty with coverage factor k=2.20, corresponding to a 95% level of confidence), as determined by qNMR. The residue weight of the MenC PS, sodium salt with 88% O-acetylation = 350.229 g/mol. Conversion factor of MenC to sialic acid or NANA: 1.132g MenC with 88 % O-acetylation = 1g sialic acid or NANA (350.229/ 309.27, MenC residue weight / Free NANA weight).

4. CONTENTS

Country of origin of biological material: United Kingdom.
Each ampoule contains the freeze-dried powder of 1 ml of MenC PS prepared in sterile MilliQ water (deionized 18.2 M Ohm). The mean mass of dry material per ampoule was 0.00063 mg as determined by weighing after freeze drying. The mean moisture content was 2.35% (Karl Fischer analysis).

5. STORAGE

Ampoules should be stored at or below -20ºC.
Please note because of the inherent stability of lyophilized material, NIBSC may ship these materials at ambient temperature.

6. DIRECTIONS FOR OPENING

DIN ampoules have an 'easy-open' coloured stress point, where the narrow ampoule stem joins the wider ampoule body. Various types of ampoule breaker are available commercially. To open the ampoule, tap the ampoule gently to collect material at the bottom (labelled) end and follow manufactures instructions provided with the ampoule breaker.

7. USE OF MATERIAL

No attempt should be made to weigh out any portion of the freeze-dried material prior to reconstitution

Re-suspend the contents of the ampoule in 1 ml of distilled water. To ensure complete solubilisation, it is advised that the material is allowed to solubilise for at least 2 hours at room temperature or 12 hours at 4ºC prior to use. The reconstituted material should be aliquoted and frozen at or below -20ºC. The standard can be used directly as a reference in physico-chemical assays or for calibrating secondary standards.

This MenC standard is 88% O-acetylated, and is appropriate for the measurement of the MenC content of material that has a similar O-acetylation level. If the standard is to be used for measuring the MenC content of a non-O-acetylated sample, or one with lower % O-acetylation, a correction factor will have to be used, following the calculation of the formula weight as listed in Annex 2 of the report for the WHO Expert Committee for Biological Standardization (ECBS). For example, for a sample with 70% O acetylation with a residue weight of 342.662, the MenC content measured with the IS will need to be corrected by multiplying the measured ug MenC PS/ml content measured by 0.978 (342.662 / 350.229). For a non-O-acetylated MenC PS, the measured ug MenC PS/ml content will need to be multiplied by 0.894 (313.236 / 350.229). The mean MenC content as determined by the resorcinol assay was 1.027 mg/ampoule.

The mean MenC content as determined by HPAEC-PAD was 1.033 mg/ampolule. Complete details of the study are given in the collaborative study report referenced in Section 9 - References. An impact assessment should be performed when implementing the use of a new standard. A conversion factor may be required depending on the current standard used and its intended use.

8. STABILITY

Reference materials are held at NIBSC within assured, temperature-controlled storage facilities. Reference Materials should be stored on receipt as indicated on the label.

Real-time and accelerated thermal degradation studies are on going. Reconstituted material stored at -20ºC up to 11 months was demonstrated to be stable. A storage time of 6 months at -20ºC is recommended for smaller aliquots of the standard after reconstitution.

9. REFERENCES

Hannah Chan, Peter Rigsby, Nicola Beresford, Timothy Rudd, Karena Burkin, Kiran Malik, Paul Matejtschuk, Alessandra Facchetti, Fang Gao, Caroline Vipond, Barbara Bolgiano and the 2nd MenC IS Working Group. Evaluation of Candidate Material for the 2nd International Standard for Meningococcal Capsular Group C Polysaccharide. WHO/BS/2023.2448. Geneva: 2023 (https://www.who.int/publications/m/item/WHO-BS-2023-2448).

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UK Official Medicines Control Laboratory

World Health Organization

10. ACKNOWLEDGEMENTS

We would like to thank the Serum Institute of India (Pune, India) for their gift of the polysaccharide used to make this standard, and to the participants and contributers to the collaborative study. See the report WHO/BS/2023.2448 for full details.

11. FURTHER INFORMATION

Further information can be obtained as follows;
This material: enquiries@nibsc.org
WHO Biological Standards:
http://www.who.int/biologicals/en/
JCTLM Higher order reference materials:
http://www.bipm.org/en/committees/jc/jctlm/
Derivation of International Units:
http://www.nibsc.org/standardisation/international_standards.aspx
Ordering standards from NIBSC:
http://www.nibsc.org/products/ordering.aspx
NIBSC Terms & Conditions:
http://www.nibsc.org/terms_and_conditions.aspx

12. CUSTOMER FEEDBACK

Customers are encouraged to provide feedback on the suitability or use of the material provided or other aspects of our service. Please send any comments to enquiries@nibsc.org

13. CITATION

In all publications, including data sheets, in which this material is referenced, it is important that the preparation's title, its status, the NIBSC code number, and the name and address of NIBSC are cited and cited correctly.

14. MATERIAL SAFETY SHEET

Classification in accordance with Directive 2000/54/EC, Regulation (EC) No 1272/2008: Not applicable or not classified

Physical and Chemical properties			
Physical appearance: Freeze dried white powder		Corrosive:	No
Stable:	Yes	Oxidising:	No
Hygroscopic:	No	Irritant:	No
Flammable:	No	Handling:	See caution, Section 2
Other (specify):	No special handling precautions		

Toxicological properties	
Effects of inhalation:	Not established, avoid inhalation
Effects of ingestion:	Not established, avoid ingestion
Effects of skin absorption:	Not established, avoid contact with skin

Suggested First Aid	
Inhalation:	Seek medical advice
Ingestion:	Seek medical advice
Contact with eyes:	Wash with copious amounts of water. Seek medical advice
Contact with skin:	Wash thoroughly with water.

Action on Spillage and Method of Disposal
Spillage of ampoule contents should be taken up with absorbent material wetted with an appropriate disinfectant. Rinse area with an appropriate disinfectant followed by water. Absorbent materials used to treat spillage should be treated as biological waste.

15. LIABILITY AND LOSS

In the event that this document is translated into another language, the English language version shall prevail in the event of any inconsistencies between the documents.
Unless expressly stated otherwise by NIBSC, NIBSC's Standard Terms and Conditions for the Supply of Materials (available at http://www.nibsc.org/About_Us/Terms_and_Conditions.aspx or upon request by the Recipient) ("Conditions") apply to the exclusion of all other terms and are hereby incorporated into this document by reference. The Recipient's attention is drawn in particular to the provisions of clause 11 of the Conditions.

16. INFORMATION FOR CUSTOMS USE ONLY

Country of origin for customs purposes*: United Kingdom * Defined as the country where the goods have been produced and/or sufficiently processed to be classed as originating from the country of supply, for example a change of state such as freeze-drying.
Net weight: 0.00063 g
Toxicity Statement: Non-toxic
Veterinary certificate or other statement if applicable. **Attached:** No

17. CERTIFICATE OF ANALYSIS

NIBSC does not provide a Certificate of Analysis for WHO Biological Reference Materials because they are internationally recognised primary reference materials fully described in the instructions for use. The reference materials are established according to the WHO Recommendations for the preparation, characterization and establishment of international and other biological reference standards http://www.who.int/bloodproducts/publications/TRS932Annex2_Inter_biolefstandardsrev2004.pdf (revised 2004). They are officially endorsed by the WHO Expert Committee on Biological Standardization (ECBS) based on the report of the international collaborative study which established their suitability for the intended use.