Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
1st International Standard for Vi polysaccharide of S Typhi
NIBSC code: 16/126
Instructions for use
(Version 6.0, Dated 25/06/2021)

1. INTENDED USE

Freeze-dried preparation NIBSC 16/126 was prepared from Vi capsular polysaccharide of S. Typhi Salmonella enterica subspecies enterica serovar Typhi (Vi PS) manufactured by GSK Bio (Rixensart Belgium). The freeze dried material has been evaluated in physico-chemical and immuno assays and qualitative and quantitative assays to assess its suitability for use as a standard for Vi PS in final fills and bulks of Vi PS typhoid vaccines [1,2]. The Vi content was determined by qNMR, gravimetry, High Performance Anion Exchange Chromatography-Pulsed Amperometric Detection (HPAEC-PAD, Hestrin assay and immuno-assays [2].

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

One ampoule contains 2.03 mg Vi PS per ampoule based on qNMR of Collaborative Study 574 [2].

4. CONTENTS

Country of origin of biological material: Belgium.
Ampoules contain a robust loose cake. One ampoule contains 2.03 ± 0.10 mg Vi PS as determined by qNMR (expanded uncertainty with coverage factor of k=2.11). By HPAEC-PAD the amount is 1.92 mg Vi PS per ampoule. O-acetylation by Hestrin is 3.24 µmole/mg Vi PS (CV 29.1%, n=10). The level of O-acetylation by qNMR is 103% (CV 3.2%, n=8). The dry weight content, determined by gravimetry is 1.70 mg (CV 9.5%, n=25), the moisture content is 4.1% (CV 16.8%, n=12) and the oxygen content is 0.35% (CV 27.6%, n=12).

5. STORAGE

Ampoules should be stored at -20 C or 4ºC
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 2.03 ml of distilled water. To ensure complete solubilisation of the material allow to dissolve for at least 2 hours at room temperature with gentle shaking followed by 12 hours/overnight at 4ºC prior to use. The standard can be used directly in physico-chemical assays or immuno assay. The reconstituted material can be aliquotted and stored at 4ºC or frozen at -20ºC or below. The standard can be used directly in physico-chemical assays, immuno assays or for calibration of secondary standards [2]. The Vi standard is fully O-acetylated (103%), and is appropriate for the measurement of the Vi content of material that has a similar level of O-acetylation. If the standard is to be used for measuring the Vi content of Vi with a lower level of O-acetylation then a correction will have to be used, following the calculation of the formula weight as listed in Annex 2 of the ECBS report [2]. For example, for a sample with 80% O-acetylation, which has a residue weight of 272.790, the Vi content measured with the IS will need to be corrected by multiplying the measured µg Vi PS/ml content measured by a factor 0.97 (= 272.790/281.196).

8. STABILITY

It is the policy of WHO not to assign an expiry date to their international reference materials.

They remain valid with the assigned potency and status until withdrawn or amended. Reference materials are held at NIBSC within assured, temperature-controlled storage facilities.
Reference Materials should be stored on receipt as indicated on the label. NIBSC follows the policy of WHO with respect to its reference materials.

Accelerated degradation studies (from -70°C to +56°C) revealed the freeze dried standard to be stable up to two years at 37°C (as determined by HPAEC-PAD to measure the Vi polysaccharide content). The freeze-dried standard (stored at -20°C) was stable up to 2.5 years (as determined by HPAEC-PAD to measure the Vi polysaccharide content). Real time and extended accelerated thermal degradation studies up to 5 years after production are on-going.
Material reconstituted at 1 mg/ml is stable for 1 year at +4°C and -20°C by HPAEC-PAD, for other assays the appropriate storage temperature for reconstituted aliquots should be determined and validated by the customer.

9. REFERENCES

1) Recommendations to assure the quality, safety and efficacy of typhoid conjugate vaccines (Replacement of WHO Technical Report Series, No. 987, Annex 3) In: WHO Expert Committee on Biological Standardization: seventy-second and seventy-third report. Geneva: World Health Organization; 2020: Annex 3 (WHO Technical Report Series, No. 1030) https://cdn.who.int/media/docs/default-source/biologicals/ecbs/post-ecbs-who-tcv-recommendations-final-3-nov-2020.pdf?sfvrsn=aeecbad0_2&download=true
2) Gao F, Swann C, Rigsby P, Lockyer K, Logan A, Rijpkema S, Bolgiano B and the Vi IS Working Group. Evaluation of two WHO First International Standards for Vi polysaccharide from Citrobacter freundii and Salmonella enterica subspecies enterica serovar Typhi. Biologicals 57:34-45 https://doi.org/10.1016/j.biologicals.2018.11.004 & WHO/BS/2017.2310 http://www.who.int/biologicals/expert_committee/BS2310_Vi_PS_Report_for_WHO_Final.pdf?ua=1

10. ACKNOWLEDGEMENTS

Drs T Pronce and O Germay of GSK Bio for donation of the Vi PS, technical assistance and support. The Coalition against Typhoid of the Albert B Sabin Vaccine Institute for financial support.

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

National Institute for Biological Standards and Control,
Potters Bar, Hertfordshire, EN6 3QG. T +44 (0)1707 641000, nibsc.org
WHO International Laboratory for Biological Standards,
UK Official Medicines Control Laboratory

World Health Organization

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

Physical and Chemical properties	
Classification in accordance with Directive 2000/54/EC, Regulation (EC) No 1272/2008: Not applicable or not Physical appearance: Off white cake	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: Yes	Irritant: No
Flammable: No	Handling: See caution, Section 2
Other (specify): N/A	
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: 0.0017 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.