Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
Bordetella Pertussis Toxin 2nd IS
NIBSC code: 15/126
Instructions for use
(Version 2.0, Dated 18/07/2018)

1. INTENDED USE

The 2nd International Standard for Bordetella Pertussis Toxin (15/126) for use in, but not limited to, the murine histamine sensitisation assay (HIST) and Chinese Hamster Ovary (CHO) cell clustering assay was established by the Expert Committee on Biological Standardisation (ECBS) of the World Health Organisation in October 2017.
The material is intended to be used in the HIST and CHO assays to determine the absence or reversion of pertussis toxin in vaccine products. 15/126 may also be suitable as a reference preparation in other methods used to measure the pertussis toxin content.

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 assigned potency for the 2nd International Standard for Bordetella pertussis toxin (15/126), agreed on the basis of an International Collaborative Study, is 1881 International Units per ampoule, determined in the HIST assay relative to the 1st International Standard for Pertussis Toxin.

Potency was also determined by CHO assay relative to the 1st International Standard in the same collaborative study. Therefore, in addition to the units assigned for HIST assays, the 2nd International Standard for Bordetella Pertussis Toxin has a potency of 680 International Units per ampoule for the CHO assay.

4. CONTENTS

Country of origin of biological material: United Kingdom.
Each ampoule contains the freeze-dried residue of 1.0ml of 0.075M potassium phosphate pH 7.6, 0.5M sodium chloride,1% trehalose and 20 micrograms pertussis toxin.

5. STORAGE

Unopened ampoules should be stored at -20°C.

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

The entire contents of each ampoule should be completely resuspended in an accurately measured amount of water or buffer solution. No attempt should be made to weigh out any proportion of the freeze dried powder. The suspension should not be frozen. The ampoules contain no bacteriostat and the preparation should not be assumed to be sterile.

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. It is the policy of WHO not to assign an expiry date to their International Reference Materials.

Accelerated degradation studies performed suggest that this material will be stable when stored at the recommended storage temperature of -20°C.
Once reconstituted, it has been confirmed that 15/126 is not stable and users are discouraged in storing the reconstituted product for later use.

Users who have any data supporting any change in the characteristics of this material are encouraged to contact NIBSC.

9. REFERENCES

1) Markey K, Asokanathan C, Tierney S, Hockley J, Douglas-Bardsley A. 2017. Collaborative Study: Evaluation of Proposed Second International Standards for Pertussis Toxin. Code: 15/126. WHO Expert Committee on Biological Standardisation. WHO/BS/2017.2315

10. ACKNOWLEDGEMENTS

Serum Institute of India is gratefully acknowledged for donation of the purified toxin material used in the preparation of the replacement standard. We would like to express our thanks to SPD (NIBSC) for assistance in the determination of freeze drying conditions and for moisture and oxygen determinations of the ampouled material and the staff of CBRM for assistance with the filling procedure. We also thank all the participants for their helpful contribution to the collaborative study.

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

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

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 powder	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: No	Irritant: Yes
Flammable: No	Handling: See caution, Section 2
Other (specify): Contains material of biological origin	
Toxicological properties	
Effects of inhalation: Avoid inhalation	
Effects of ingestion: Avoid ingestion	
Effects of skin absorption: 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. Remove contact lenses if suitable and possible.	
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: 0.5 - 1.0 g
Toxicity Statement: 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.