Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
3rd IS for Diphtheria Toxoid for use in Flocculation Test
NIBSC code: 13/212
Instructions for use
(Version 2.0, Dated 26/10/2015)

1. INTENDED USE

The 3rd International Standard for Diphtheria Toxoid for use in Flocculation Test (13/212) was established by the Expert Committee on Biological Standardization of the World Health Organisation in October 2015. The material is intended to be used for standardization of flocculation assay to determine the Lf content of diphtheria toxoid.

13/212 may also be suitable as a reference preparation in other methods used to measure the Lf content of diphtheria toxoid, such as ELISA or SRD.

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 unitage for 13/212 is 1870 Lf per ampoule. This is based on the results of flocculation tests performed by 25 laboratories in 15 different countries [1].

4. CONTENTS

Country of origin of biological material: Denmark.
Bulk purified diphtheria toxoid was kindly donated by Statens Serum Institut (Copenhagen). The bulk toxoid, 2141 Lf/mg protein nitrogen, was stabilised by the addition of sodium chloride (final concentration 0.1 M) and trehalose (final concentration 1% w/v). Filling and freeze-drying was performed at NIBSC in November 2013. The average dry weight of the ampoule contents is 0.03 g (CV 0.62%) and the mean residual moisture content was determined as 0.38% (CV 15.27%).

5. STORAGE

Store in the dark 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

No attempt should be made to weigh out any portion of the freeze-dried material prior to reconstitution
The entire contents of one ampoule should be completely re-suspended in 1 ml of a suitable solution (saline is suitable).

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 highly stable when stored at the recommended storage temperature of -20°C, and the assigned unitage remains valid until the material is withdrawn or replaced.

Once reconstituted, 13/212 has been confirmed to be stable for up to 3 months following storage at +4°C. However, users are encouraged to determine the stability of the material according to their own methods of preparation, storage and use.

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

9. REFERENCES

1. Coombes L, Rigsby P, Sesardic D, Stickings P. 2015. Collaborative Study: Calibration of Replacement International Standard for Diphtheria Toxoid for use in Flocculation Test. WHO Expert Committee on Biological Standardization. WHO/BS/2015.2254

10. ACKNOWLEDGEMENTS

Statens Serum Institut is gratefully acknowledged for donation of the purified toxoid material used in the preparation of the replacement standard. All participants of the collaborative study performed to calibrate this replacement standard are gratefully acknowledged.

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 toxoid		Corrosive:	No
Stable:	Yes	Oxidising:	No
Hygroscopic:	No	Irritant:	No

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WHO International Laboratory for Biological Standards,
UK Official Medicines Control Laboratory

World Health Organization

Flammable:	No	Handling:See caution, Section 2
Other (specify):	Contains material of bacterial origin	
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: 0.03 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.