Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
2nd International Standard for Diphtheria Antitoxin Equine
NIBSC code: 18/180
Instructions for use
(Version 2.0, Dated 22/11/2021)

1. INTENDED USE

The 2nd International Standard for Diphtheria Antitoxin Equine was established by the Expert Committee on Biological Standardization of the World Health Organisation in October 2021 and replaces the 1st International Standard (DI).

This antitoxin preparation is suitable for use as the reference diphtheria antitoxin in toxin neutralisation tests (in vivo and in vitro) that are used to measure potency of equine diphtheria antitoxin, but is primarily intended for calibration of secondary standards. For measurement of diphtheria antitoxin in human serum, customers should use the International Standard for Diphtheria Antitoxin Human (NIBSC code 10/262).

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

Each ampoule contains 57 International Units. This value was assigned in a multi-laboratory collaborative study using the results obtained in toxin neutralisation assays in vivo and in vitro [1].

4. CONTENTS

Country of origin of biological material: Japan.
Bulk refined diphtheria immunoglobulin prepared from horses immunised with diphtheria toxoid was obtained from The Chemo-Sero-Therapeutic Research Institute (Kaketsuken), Japan. The bulk material was diluted in phosphate buffered saline and freeze-dried (1ml per ampoule) at NIBSC in October 2018.

5. STORAGE

Ampoules should be stored 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 contents of each ampoule should be reconstituted in sterile water. Reconstitution of 1 ampoule with 1 ml water will provide a solution of 57 IU/ml. Other solvents for reconstitution may also be suitable but this should be determined by the end user.

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. Accelerated degradation studies conducted at NIBSC suggest that this material will have good long term stability [1] and evidence obtained with other dried serum standards suggests that they undergo negligible loss of activity during long term storage when stored at the recommended temperature [2].

9. REFERENCES

[1]https://cdn.who.int/media/docs/default-source/biologicals/call-for-comments/bs.2021.2407_who-2nd-is-diphtheria_antitoxin_equine.pdf?sfvrsn=658f8a06_5
[2] Jerne NK and Perry WLM. The stability of Biological Standards, Bull. Wld. Hlth. Org. 1956, vol. 14 pp 167-182

10. ACKNOWLEDGEMENTS

NIBSC is grateful to the participants in the collaborative study who provided data to support the calibration and establishment of this reference preparation [1]

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: White lyophilised cake		Corrosive:	No
Stable:	Yes	Oxidising:	No
Hygroscopic:	No	Irritant:	No
Flammable:	No	Handling:	See caution, Section 2
Other (specify):	None		

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

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

World Health Organization

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*: Japan * 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: Mean dry weight 6.1 mg; total weight per ampoule 3.68 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.