



**WHO International Standard
Diphtheria Antitoxin Equine DI.
NIBSC code: 16/166
Instructions for use
(Version 1.0, Dated 12/08/2016)**

1. INTENDED USE

The International Standard (dried horse serum) was prepared and characterised by the Statens Serum Institut (SSI), Copenhagen, Denmark (see enclosed package insert from SSI for details [1]). With effect from 1st July 1997, the National Institute for Biological Standards and Control (NIBSC), Potters Bar, UK is the custodian and distributor of this material.

This standard preparation is distributed as a dilution of the dried horse serum prepared at NIBSC in 66% glycerol in normal saline. A liquid fill is prepared from the original dried material approximately every 2 years. The current preparation coded 16/166 was prepared and filled on 22 June 2016 and replaces the previous preparation coded 14/266.

This antitoxin preparation is suitable for use as the reference diphtheria antitoxin in toxin neutralisation tests in vivo and in vitro, 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].

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 concentration of diphtheria antitoxin in the final liquid preparation is 10 IU/ml. The International Unit for Diphtheria Antitoxin is defined as the activity contained in 0.0628 mg of the dried serum (see package insert from SSI).

4. CONTENTS

Country of origin of biological material: Denmark.
The standard preparation is distributed as a solution of dried hyperimmune horse serum in 66% v/v glycerol in saline (approximately 10 ml per vial). The concentration of diphtheria antitoxin is 10 IU/ml.

5. STORAGE

The preparation should be stored in the dark at +4°C.

6. DIRECTIONS FOR OPENING

Vials have a 'flip-up' circular cap. Either on the cap or the collar of the vial, there is an indication of the point at which to lever off the cap. This exposes an area of the stopper through which reconstitution and withdrawal of the preparation can be made using a hypodermic needle and syringe. If use of a pipette is preferred, then fully remove the metal collar using, for example, forceps, taking care to avoid cuts by wearing appropriate gloves. Remove the stopper for access. Care should be taken to prevent loss of the contents.

7. USE OF MATERIAL

The ampoules contain no bacteriostat or preservative. Vial contents should be mixed by inversion before use and the required quantity can be removed by inserting a hypodermic needle with syringe through the rubber stopper.

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.

The results of in-house potency testing using a toxin neutralisation test suggest that the potency of the liquid preparation of DI can be assumed to be stable for up to 2.5 years from the date of reconstitution and fill, when stored as indicated.

Users who have data supporting any deterioration in the characteristics of any reference preparation are encouraged to contact NIBSC.

9. REFERENCES

[1] Insert from SSI attached as an appendix to this IFU

[2] <http://www.nibsc.ac.uk/documents/ifu/10-262.pdf>

10. ACKNOWLEDGEMENTS

N/A

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.

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.

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: Viscous liquid, colourless, clear	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: No	Irritant: No
Flammable: No	Handling: See caution, Section 2
Other (specify): Contains horse serum and 66% glycerol	
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: 10.8 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_bi_olefstandardsrev2004.pdf (revised 2004). They are officially endorsed



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STATENS
SERUM
INSTITUT

prevention and control
of infectious diseases
and congenital disorders

THE INTERNATIONAL STANDARD
for
DIPHTHERIA ANTITOXIN
(1st international standard preparation)

1. THE STANDARD PREPARATION

The history of this standard is not entirely clear. Apparently¹ a standard preparation existed from 1922 but there is no information on the way in which the International Unit was defined. The present standard was prepared in Copenhagen in 1934 and is the first preparation with a clearly defined unitage. The standard is a hyperimmune horse serum dried by means of P₂O₅, in 5 ml aliquots in ampoules. The International Unit for Diphtheria Antitoxin is defined as the activity contained in 0.0628 mg of the dry material in these ampoules.

2. AMPOULE CONTENTS

The standard preparation is distributed as a solution of the dried serum in 66% v/v glycerol in saline. The concentration is 10 IU/ml.

3. USE OF THE STANDARD

To be used for calibrating local reference sera.

4. GENERAL REMARKS ABOUT INTERNATIONAL REFERENCE MATERIALS

International biological standards and international biological reference reagents provide a means of ensuring uniformity throughout the world in the designation of the potency or activity of preparations used in the prophylaxis, therapy, or diagnosis of disease, where this cannot be expressed in terms of physical or chemical quantities. The International Units are units of quantities of "effective constituent"².

The standard is the material as it exists in the ampoules; the "material" thus includes the effective constituents together with all the other constituents that may be present (moisture, carrier, buffer, salt etc., according to the form in which the standard is available).

DI

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International biological reference materials are intended for use in the calibration of the contents of "effective constituent" in national or working standard preparations and for the expression of these contents in the respective International Units. For the routine use in the laboratory the national or working standards should be used in order to save as much as possible the international reference materials. These are only sent to individual laboratories in very limited amounts. International Reference Materials are distributed free of any charge to National Control Laboratories of Member States of the World Health Organization. Other laboratories are due to pay a handling charge.

October 1996

5. REFERENCES

1. Gautier, R, The Health Organisation and Biological Standardization, Quart. Bull. Health Organ. L.O.N., Vol. 4, p. 499, 1935.
2. Jerne & Wood, The Validity and Meaning of the Results of Biological Assays, Biometrics vol. 5, December 1949.

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