Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
The 1st International Standard for Diphtheria (Schick) Test Toxin
NIBSC code: STT
Instructions for use
(Version 8.0, Dated 14/05/2018)

1. INTENDED USE

This material has been prepared and characterised by the Statens Serum Institut (SSI), Copenhagen, Denmark. 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.

For details of this International Standard, please refer to the enclosed package insert from the Statens Serum Institut.

2. CAUTION

This preparation is not for administration to humans or animals in the human food chain.

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.

Diphtheria toxin is highly toxic with a reported lethal dose of approximately 0.1 µg/Kg of body weight. This material should be handled with care by trained and competent laboratory staff. It is recommended that staff working with this material have an anti-diphtheria antibody level >0.1 IU/ml (when measured by ELISA).

3. UNITAGE

The total contents of one ampoule contains 900 International Units (IU) of Diphtheria (Schick) Test Toxin. Please see enclosed package insert from SSI for full details.

4. CONTENTS

Country of origin of biological material: Denmark.

Please see enclosed package insert from SSI for full details on ampoule contents. This product contains bovine albumin as an excipient.

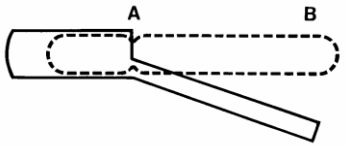
5. STORAGE

Reference materials should be stored on receipt as indicated on the label.

Please note: because of the inherent stability of lyophilized material, NIBSC may ship these materials at ambient temperature.

6. DIRECTIONS FOR OPENING

Tap the ampoule gently to collect the material at the bottom (labelled) end. Ensure ampoule is scored all round at the narrow part of the neck, with a diamond or tungsten carbide tipped glass knife file or other suitable implement before attempting to open. Place the ampoule in the ampoule opener, positioning the score at position 'A'; shown in the diagram below. Surround the ampoule with cloth or layers of tissue paper. Grip the ampoule and holder in the hand and squeeze at point 'B'. The ampoule will snap open. Take care to avoid cuts and projectile glass fragments that enter eyes. Take care that no material is lost from the ampoule and that no glass falls into the ampoule.



Side view of ampoule opening device containing an ampoule positioned ready to open. 'A' is the score mark and 'B' the point of applied pressure.

7. USE OF MATERIAL

No attempt should be made to weigh out any portion of the freeze-dried material prior to reconstitution.

Refer to the attached insert from SSI.

8. STABILITY

Reference materials are held at NIBSC within assured, temperature-controlled storage facilities. It is the policy of the WHO not to assign an expiry date to their international reference materials. The units assigned to this material were valid at the time of establishment and they remain valid with the assigned potency and status until withdrawn or amended. There is no data on long term stability.

Once ampoule contents are reconstituted, users should determine the stability of the material according to their own method of preparation, storage and use.

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

9. REFERENCES

1. WHO Technical Report Series No. 96, 1955, 7.

2. WHO Technical Report Series No. 61, 1953, 57 ff.

3. Gill, DM. Bacterial toxins: a table of lethal amounts. Microbiological Reviews. 1982; 46(1): 86-94.

3. Jerne & Wood, The Validity and Meaning of the Results of Biological Assays, Biometrics vol. 5, December 1949.

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

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

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 powder	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: No	Irritant: No
Flammable: No	Handling: See caution, Section 2
Other (specify):	Contains material of bacterial origin
Toxicological properties	
Effects of inhalation:	Toxic by inhalation (R23)
Effects of ingestion:	Toxic if swallowed (R25)
Effects of skin absorption:	Toxic if adsorbed through skin (R24)
Suggested First Aid	
Inhalation:	Remove to fresh air; seek medical advice if breathing becomes difficult
Ingestion:	Wash out mouth with water and administer fresh water provided person is conscious. Seek medical advice.
Contact with eyes:	Flush with copious amounts of water for at least 15 min. Seek medical advice.
Contact with skin:	Flush with copious amounts of water and soap for at least 15 min. Remove contaminated clothing.
Action on Spillage and Method of Disposal	
Spillage of ampoule contents should be taken up with absorbent material wetted with an appropriate cleaning solution (chloros or sodium hydroxide solution is suitable). Rinse area with the cleaning solution follwed by soap and 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*: Denmark. * 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: 1 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.

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STATENS SERUM INSTITUT
prevention and control of infectious diseases and congenital disorders

THE INTERNATIONAL STANDARD for DIPHTHERIA (SCHICK) TEST TOXIN (1st international standard preparation)

1. THE STANDARD PREPARATION

The standard preparation was established in 1954[1]. It is prepared from a batch of purified diphtheria toxin. The toxin was produced in the Vaccine Department, Statens Serum Institut, Copenhagen in 1951 and was known as lot no. 8/51. For details of production see[2]. 20 stock ampoules each containing about 3100 Lf of toxin freeze-dried from a solution containing 10 mg bovine albumin and 1.1 mg KH_2PO_4 were made.

2. AMPOULE CONTENTS

One stock ampoule (amp. "A") was redissolved in 3.4 litre of solution of a phosphate buffer, pH 7.3 containing 1 g of bovine albumin per litre. This solution was filled into ampoules (1 ml/ampoule) and freeze-dried. By definition[1], the total contents of one ampoule contains 900 International Units (IU) of Diphtheria (Schick) Test Toxin.

The standard preparation distributed for the time being was made in the same way in 1975 from a second stock ampoule. The potency was controlled in two laboratories but the results have never been published.

3. USE OF THE STANDARD

The standard preparation defines the IU and might be used to potency assay other Schick toxins in these units.

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"[3].

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).

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. The preparations are sent free of charges but sometimes a small charge might be claimed for the air-freighting.

November 1996

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