Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
4th WHO International Standard for Tetanus Toxoid Adsorbed
NIBSC code: 08/218
Instructions for use
(Version 6.0, Dated 29/10/2014)

1. INTENDED USE

The 4th International Standard is the primary biological standard for use in tetanus potency assays.

This standard has separate units assigned for assays performed using guinea pigs and mice (see section 3).

2. CAUTION

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

Polygeline used in formulation of the standard contains gelatine. This is a non-UK source of material of bovine origin and is in a product licenced for human clinical use 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, agreed on the basis of an International Collaborative Study, is 490 International Units of biological activity per ampoule, determined in guinea pig challenge assays relative to the 3rd International Standard for Tetanus Toxoid, Adsorbed [2].

Potency was also determined by mouse challenge assay relative to the 3rd International Standard in the same collaborative study [2]. At a meeting held in October 2012, the WHO Expert Committee on Biological Standardization adopted a proposal to assign IU to the International Standard based on the results of these mouse challenge assays. Therefore, in addition to the units assigned for guinea pig assays, the 4th International Standard for Tetanus Toxoid Adsorbed has a potency of 260 IU/ampoule for mouse assay.

4. CONTENTS

Country of origin of biological material: Switzerland.
Each ampoule contains 1 ml of freeze-dried tetanus toxoid, adsorbed, formulated 1:1 with polygeline.

5. STORAGE

Unopened 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 entire contents of each ampoule should be completely resuspended in an accurately measured amount of suitable solution (e.g. 0.9% NaCl). It is recommended that the suspension is used on the same day after reconstitution. The suspension should not be frozen.

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 [3] suggest that this material will be suitably stable when stored at the recommended storage temperature of -20°C, and the assigned potency value remains valid until the material is withdrawn or replaced.

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

9. REFERENCES

1. This standard was produced under WHO guidelines cited in the WHO Technical Report Series, No. 927, 2005.

2. Tierney R, Hockley J, Rigsby P, Sesardic D. International collaborative study: calibration of replacement WHO international standard for tetanus toxoid adsorbed. WHO Expert Committee on Biological Standardisation; 2010. Ref: BS/10.2150.

3. Tierney R, Stickings P, Hockley J, Rigsby P, Iwaki M, Sesardic D. Collaborative study for the calibration of a replacement International Standard for Tetanus Toxoid Adsorbed. Biologicals. 2011; 39 (6): 404-416.

10. ACKNOWLEDGEMENTS

Swiss Serum Institute 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

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:	Yes	Irritant:	No
Flammable:	No	Handling:	See caution, Section 2
Other (specify):	Source of material: Bacterial (C. tetani)		

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 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: 1 ml
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.