Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO Reference Reagent
WHO International Reference Reagent Tetanus Antitoxin Equine for use in Flocculation Test
NIBSC code: 21/230
Instructions for use
(Version 3.0, Dated 06/03/2024)

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1. INTENDED USE

This material is a freeze-dried preparation of hyperimmune horse tetanus antitoxin. It is intended for use as a reagent (not a calibrant) in the in vitro flocculation (Lf) assay for tetanus toxoid [1, 2]. When used in the flocculation assay, the Lf equivalent (Lf-eq) value must be determined in-house, against the WHO IS tetanus toxoid (16/302). The equine antitoxin was prepared by repeated immunisation of horses with tetanus toxoid/toxin, followed by F(ab)2 purification.

2. CAUTION

The material is not of human or bovine origin. This preparation is not for administration to humans or animals

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

There are no units assigned to this reagent - it must be pre-calibrated for use in the flocculation test in Lf-eq against the WHO IS Tetanus Toxoid for use in Flocculation Test (16/302) within each laboratory. However, to aid users with preparation of the dilutions of the antitoxin in the flocculation test, we provide a nominal value of 1400 International Units (IU) per ampoule of horse tetanus antitoxin (determined in a single lab).

4. CONTENTS

Country of origin of biological material: Germany.
Each ampoule contains the freeze-dried residue of 1.0 ml horse antitoxin. The source material was obtained from Wirtschaftsgenossenschaft deutscher Tierärzte (WDT), Germany.

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

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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.

NIBSC follows the policy of WHO with respect to its reference materials.

9. REFERENCES

1. Tierney, R., Hockley, J., Rajagopal, S., Stickings, P. 2019. Collaborative Study: Calibration of Replacement International Standard for Tetanus Toxoid for use in Flocculation Test. WHO Expert Committee on Biological Standardization. WHO/BS/2019.2369

2. Rajagopal, S., Tierney, R., Rigsby, P., Stickings, P. 2022. Collaborative Study: Calibration of 1st WHO Reference Reagent for Tetanus Antitoxin Equine for use in Flocculation Test. WHO Expert Committee on Biological Standardization. WHO/BS/2022.2431.

10. ACKNOWLEDGEMENTS

Not applicable.

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.

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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

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 freeze-dried powder		Corrosive:	No
Stable:	Yes	Oxidising:	No
Hygroscopic:	Yes	Irritant:	Unknown
Flammable:	No	Handling: See caution, Section 2	
Other (specify):	Contains material of biological origin and ≤0.5% phenol		

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: 0.035g
Toxicity Statement: Toxicity not assessed
Veterinary certificate or other statement if applicable. **Attached:** Yes WDT Certificate

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.

WDT
Das Tierarztunternehmen.

Serumwerk Memsen

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To whom it may concern

HEALTH CERTIFICATE

We hereby confirm that all horses used for the production of Tetanus antiserum, batch No. 750, Date of Manufacturing: 07/2019, have been in clinically good health condition and did not show signs of systemic infectious disease during a period of 8 days before and 3 days post bleeding.
Blood samples were taken at the installing examination and tested negative for infectious anaemia, dourine and glanders at the State Office for Consumer Protection and Food Safety. Origin of all horses is the European Community.
The horses are branded with an unchangeable stable number. Horses with the following numbers were integrated in the production of the current batch: 278, 283, 286, 291, 293, 294, 295, 301, 315, 318, 322, 326, 328, 329, 330, 331, 332, 333, 336, 337, 340, 344, 345, 346, 347, 348

On behalf of
Serumwerk Memsen, Hoyerhagen

19.08.2019

Dr. Silke Kräft
(Qualified Person)

WDT
Das Tierarztunternehmen.

Serumwerk Memsen

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Declaration regarding Viral Safety

We herewith confirm that ***Tetanus antiserum batch No. 750,*** manufactured from raw serum batch No. 729, complies with the following specifications (for method and duration see annex 1):

- no cytopathogenic virus detectable
- hemagglutination-test/ hemadsorption-test negative
- immunocytochemical examination for exclusion of EHV-1, EHV-4 and EAV

Testing has been performed by MICROMUN Privates Institut für Mikrobiologische Forschung GmbH, Greifswald.

Hoyerhagen, 19.08.2015

Dr. Silke Kräft
(qualified person)