Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

Non WHO Reference Material
Botulinum Type A Antitoxin, Equine
NIBSC code: 14/174
Instructions for use
(Version 2.0, Dated 17/05/2018)

This material is not for in vitro diagnostic use.

1. INTENDED USE

This material is the freeze-dried residue of hyperimmune monovalent horse antiserum to Clostridium botulinum type A toxin. It is intended for calibration of the bioassay for botulinum type A antitoxin. The material may also be suitable to confirm serotype identity of botulinum type A toxin. No cross-neutralization with serotypes B, C, D, E, F or G was confirmed in three laboratories using different test methods (mouse lethality, local flaccid paralysis, or ex vivo mouse phrenic nerve methods) using thousand-fold, or greater, excess of antitoxin, 14/174. This material is an alternative to non WHO reference Botulinum type A antitoxin, equine, coded 59/021, which did show cross-neutralization with type B toxin at high concentrations.

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 material is an alternative for non WHO Reference Material for Botulinum type A antitoxin, coded 59/021 [1], which was calibrated relative to the 1st WHO International Standard (60/18, BTUSA). Testing at NIBSC by local paralysis assay, relative to 59/021, indicated activity of 1250 IU/ampoule.

4. CONTENTS

Country of origin of biological material: United States.
The bulk material was characterized [2] and donated to NIBSC in March 2012 by Dr. J.E. Keller of FDA, CBER Office of Vaccines Research and Review, Bethesda MD, USA. On 21 November 2014, hyperimmune horse serum was filtered, and 1.0 ml filled into 5.0 ml ampoules and freeze-dried at NIBSC Standards Processing Division. Four days later, ampoules were overlaid with nitrogen and sealed. The preparation contains the freeze-dried residue of 1.0 ml of undiluted horse serum.

5. STORAGE

Unopened ampoules should be stored 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

Clostridium botulinum antitoxins were established to define International Units for each serotype of antitoxin to be used in the control of therapeutic antitoxin preparations. Preparation and assay of the International Standards for Clostridium botulinum antitoxin types A, B, C, D and E were described by Bowner [3]. This material, traceable in IU to BTUSA, is intended for calibration of the bioassay for botulinum type A antitoxin. The material may also be suitable to confirm type A serotype identity.

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.

Units assigned to this material were valid at the time of calibration and there is no data available on long-term stability. However, freeze-dried serum standards are expected to undergo negligible loss of activity during long-term storage at the indicated storage temperature [4].

Once 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 changes in the characteristics of this material are encouraged to contact NIBSC.

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

9. REFERENCES

1. Jones RGA, Corbel MJ and Sesardic D. A review of WHO International Standards for botulinum antitoxins. Biologicals, 2006: 34; 223-226.

2. Li D, Matoo P and Keller J.E. New equine antitoxins to botulinum serotypes A and B. Biologicals, 2012: 40; 240-246.

3. Bowner EJ. Preparation and assay of the International Standards for Clostridium botulinum types A, B, C, D and E antitoxins. Bull World Health Organization, 1963: 29; 701-709.

4. Jerne NK and Perry WLM. The stability of biological standards. Bull World Health Organization, 1956: 14; 167-182.

10. ACKNOWLEDGEMENTS

Dr. J.E. Keller of FDA, CBER, Bethesda MD, USA for donation of hyperimmune monovalent antitoxin.

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

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

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:	Yes	Irritant:	No
Flammable:	No	Handling:	See caution, Section 2
Other (specify):	Contains equine serum		

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: Approx. 100 mg
Toxicity Statement: Non-toxic
Veterinary certificate or other statement if applicable**.** **Attached:** No