Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO Reference Reagent
Clostridium perfringens Beta toxoid 1st International Reference Preparation
NIBSC code: CWBETATD
Instructions for use
(Version 10.0, Dated 23/01/2024)

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1. INTENDED USE

The International Reference Preparation of Clostridium welchii (perfringens) Beta Toxoid was established in 1975 by the Central Veterinary Laboratory, UK [1]. The toxoid is intended to be used for the standardization of vaccines containing this component. The International Standard for Clostridium welchii (perfringens) Type B Antitoxin, Equine has subsequently been re-named as the International Standard for Clostridium perfringens Beta Antitoxin, Equine [2].

2. CAUTION

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

Not human or bovine source material
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

No International units have been assigned to this preparation.

4. CONTENTS

Country of origin of biological material: United Kingdom.
The International Reference Preparation was prepared from cultures of Cl. welchii (perfringens) by treatment with formalin and filtration. The toxoid was concentrated by precipitation with ammonium sulphate. The concentrated toxoid was dispensed in 1.0ml volumes in ampoules and freeze-dried in an atmosphere of dry nitrogen. The average weight of dry material per ampoule was determined as 0.0692g ± 0.0038g for the beta toxoid.

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

Old style ampoule

7. USE OF MATERIAL

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

a). Reconstitution of Reference Preparation
One ampoule of the reference preparation is reconstituted in 1.0ml of distilled water. Care should be taken to ensure that the entire ampoule contents are completely resuspended.
b). Preparation of Reference Vaccine
18ml of physiological saline containing sufficient thiomersalate to ensure 0.01% concentration in the complete vaccine, and 5ml of sterile aluminium hydroxide gel (2%) are thoroughly mixed and the contents of 2 of the reconstituted ampoules of reference toxoid are added to the 23ml of the diluted aluminium hydroxide, giving a total volume of 25ml. The traces of toxoid remaining in the ampoules are washed out by transferring volumes of the mixture to and from the ampoules several times using a Pasteur pipette and mixing thoroughly after each transfer. The vaccine is allowed to adsorb at room temperature for three days, shaking at intervals to ensure a homogeneous vaccine.
c). Preparation of Dilutions of the Reference Vaccine
The reference vaccine is diluted in a diluent consisting of 1 part of aluminium hydroxide gel (2%) and 4 parts of physiological saline. Dilutions are prepared in five-fold steps i.e. 1/5, 1/25, 1/125. The use of this diluent retains a constant percentage of adjuvant. Both the initial mixture and the dilutions should be prepared fresh each time material is required for injection.
d). The Potency Test
It is suggested that groups of not less than ten rabbits should be used for each vaccine dilution. A volume of 2ml of vaccine is injected by the subcutaneous route on two occasions with an interval of 21-28 days between injections. The animals are bled 14 days after the second injection and the sera are either pooled as a bulk sample or combined in several pools, depending on the assay design.
e). Interpretation of Results
The results of the assays on which the toxoid was established as an International Reference Preparation showed that estimates of potency of test vaccine preparations varied widely within and between laboratories, using this particular assay method. However it was found that, by combining all the collaborative assay results at each dilution level, a dose response curve could be demonstrated. The role of the International Reference Preparation at this stage is therefore to provide a stable reference preparation to use in checking test systems.

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.

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.

9. REFERENCES

1. WHO Expert Committee on Biological Standardization Twenty-seventh Report. World Health Organization Technical Report Series 1976; 594; p14.
WHO/BS/75.1122.

2. WHO Technical Report Series 1982; 673; p19.

10. ACKNOWLEDGEMENTS

This material was prepared and characterised by the Veterinary Laboratories Agency, Weybridge, Surrey, UK.

11. FURTHER INFORMATION

Further information can be obtained as follows;
This material: enquiries@nibsc.org
WHO Biological Standards:

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

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

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 material of bacterial origin treated with formalin	
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. 0.0692g
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.