Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
Anti-Brucella abortus Serum, Bovine
NIBSC code: 2BADS
Instructions for use
(Version 10.0, Dated 14/06/2017)

1. INTENDED USE

This material has been prepared and characterised by the Veterinary Laboratories Agency (VLA), Weybridge, Surrey, UK. With effect from 1st June 1998, 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 Veterinary Laboratories Agency. The Distribution statement in the package insert is no longer valid.

The package insert from the VLA is attached.

2. CAUTION

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

The material is of bovine origin. The material is certified to be obtained from animals taken from a closed herd in the female line since 1980, in which no animal has been clinically suspected of having BSE & which has not been fed rations containing ruminant derived protein during that period. 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

One ampoule contains 1000 IU agglutinating activity and 1000 IU complement fixing activity. Assigned content of vial valid at time of manufacture – no information on long term stability.

4. CONTENTS

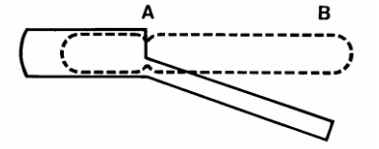
Country of origin of biological material: United Kingdom.
See attched insert from the VLA.

5. STORAGE

Each ampoule can be reconstituted for example with 1 mL of water for injection or a diluent that will not affect the pH.
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.

8. STABILITY

It is the policy of WHO not to assign an expiry date to their international reference materials. They remain valid with the assigned potency and status until withdrawn or amended.
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.

Once reconstituted, diluted or aliquoted, 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

N/A

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

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

Physical and Chemical properties			
Classification in accordance with Directive 2000/54/EC, Regulation (EC) No 1272/2008: **Not applicable or not cla** 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 bovine origin.		
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: 0.1 g
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.

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CVL

SECOND INTERNATIONAL STANDARD FOR ANTI-BRUCELLA ABORTUS SERUM (BaDS2)

Description

The second International Standard for Anti-Brucella abortus Serum was established in 1968 and replaced the first International Standard, stocks of which were almost exhausted. It is intended for standardizing the measurement of agglutinating and complement-fixing activity in sera.

It was prepared from the serum of a cow which has been infected experimentally with Br.abortus biotype 1, strain 544 (FAO/WHO reference strains) six years previously and which had remained infected throughout this time. The serum was diluted to a suitable titre with Brucella - negative bovine serum. The diluted serum was distributed in 1ml volumes into neutral - glass ampoules and freeze-dried. The ampoules were filled with nitrogen at about atmospheric pressure and sealed.

The average weight of dried material in each ampoule has been determined as 95.52mg with a standard deviation of 3.04%.

The antibodies in the Standard have been shown to consist almost entirely of immunoglobulin G.

International Units

Each ampoule has been assigned a unitage of 1,000 International Units of agglutinating activity and 1000 International Units of complement-fixing activity.

Both International Units are defined as the activity contained in 0.09552mg of the International Standard.

Distribution

The International Standard is distributed by the International Laboratory for Biological Standards, Ministry of Agriculture, Fisheries and Food, Central Veterinary Laboratory, New Haw, Addlestone, Surrey, England, on behalf of the World Health Organization. It is available free of charge in limited amounts. If a laboratory needs more than one ampoule every six months, it is expected to prepare its own standard and to calibrate it against the International Standard.

Reconstitution of the International Standard

The Standard should be reconstituted immediately before it is to be used.

Ampoules may be opened by scoring with a small saw specifically designed for the purpose, or a hard mineral edge, for approximately one third of the circumference. Application of a piece of red hot glass rod to this scratch will give a clean line of fracture.

If the scoring is made firmly and the glass rod is hot enough, it is possible to produce a fine crack without disturbing the ampoule top until needed. Then slight pressure will complete the separation.

The freeze-dried material in each ampoule may be reconstituted in any convenient volume of a suitable diluent, which will not alter the final pH.

Care should be taken to ensure that the entire contents of the ampoule are completely resuspended. This can be achieved by suspending the bulk of the contents of the ampoule in some of the fluid, and using the remainder of the diluent to rinse out the ampoule three times.

A low dilution of the Standard, e.g. 1/50, in a suitable preservative, e.g. 0.5 (v/v) phenol in physiological saline, may be stored at about 4°C for up to six months without detectable loss of potency.

National and Laboratory Standards

National and laboratory standards should be prepared in a stable form. This may be achieved by freeze-drying aliquots of the reference preparation in neutral-glass ampoules and sealing them in an oxygen-free atmosphere by fusion of the glass. The ampoules should be stored in the dark at a low temperature, e.g. -20°C.

If such a standard is to be used to measure both agglutinating and complement-fixing activity, it is essential that it be calibrated independently by both agglutination and complement-fixation tests. This is done by performing a series of tests by each method to compare simultaneously the activity of the new standard with that of the International Standard.

After determining the titres of the two sera approximately, the tests should be repeated using dilutions closely spaced around the expected end-point. For example, if the expected agglutination end-point is 1/500, dilutions of 1/300, 1/400, 1/500, 1/600 and 1/700 may be used. If the expected complement-fixation end-point is 1/200, dilutions of 1/120, 1/160, 1/200, 1/240 and 1/280 may be used. The dilutions should cover the range from complete agglutination or fixation to no agglutination or fixation.

The relative agglutinating and complement-fixing estimates of the two sera should be estimated by the usual statistical methods. The number of International Units of each activity per ampoule of the proposed standard can thus be calculated. This calculation should be based on a series of at least three tests of each activity.

Alternatively, two standards can be prepared, one for the agglutination test and one for the complement-fixation test, and each calibrated by the corresponding test.

It is suggested that the potency of a national or laboratory standard should be checked against that of a fresh sample of the International Standard about once a year.

The International Laboratory for Biological Standards at Weybridge is willing to advise and assist laboratories in providing their own standards.

Routine Tests

Standard sera can be used to standardize agglutination and complement-fixation tests in the following ways:

1) **Standardization of antigens.** Each batch of antigen is titrated against the standard serum. The amount of antigen to be used in routine tests is that which gives 50% agglutination or fixation with a pre-selected number of International Units of serum of pre-selected dilution of standard. The number of International Units selected for this purpose varies from one laboratory to another but is usually between one and four.

   For example, if 2 I.U. is chosen for the agglutination test and if the standard contains 1000 I.U. of agglutinating activity per ml., the antigen should give 50% agglutination with a 1/500 dilution of the standard, i.e., a dilution of 1/500 after the addition of antigen assuming that the final volume in each agglutination tube is 1ml.

2) **Control of routine tests.** To check that the test conditions have remained constant, the standard serum is titrated along with every batch of tests. This also enables the potency of the sera being tested to be expressed in International Units by comparing their titres with that of the Standard.

The criteria for interpreting the results of test for diagnosis in man and in animals are given in the Fourth Report of the FAO/WHO Expert Committee on Brucellosis (WHO Technical Report Series 289). It should be noted, however, that countries lay down their own criteria of levels of I.U. of antibody accepted as negative and the country's requirements should be considered.