Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO Reference Reagent
Pertussis Antiserum (Human) 1st RR
NIBSC code: 06/142
Instructions for use
(Version 2.0, Dated 09/04/2013)

1. INTENDED USE

Serological analysis by Enzyme-linked immunosorbent assays (ELISAs) has been widely used for evaluation of antibody responses to pertussis vaccination and infection. Serum Reference Standards are essential for comparison of both intra- and inter-laboratory estimates. The freeze-dried anti-serum (ampoule code 06/142) was prepared from sera kindly donated by Dr Carl Heinz Wirsing von König, Institut für Infektiologie Krefeld GmbH (IIK), Krefeld, Germany. On behalf of WHO and in collaboration with members from CBER, FDA, USA and Institut für Infektiologie Krefeld GmbH, Germany , a collaborative study to compare the candidate material with the US reference preparations lot 3, lot 4 and lot 5 was organized by NIBSC in 2007. Twenty-two laboratories from 15 countries participated in this study. ELISA's for IgG anti-PT, anti-FHA and anti-69kDa were carried out by the participants. Data from the study showed that comparison of the antibody activity of preparation 06/142 in terms of the First International Standard (06/140) and the relevant US reference lot were in good agreement among laboratories. Results from assays of the candidate material after storage for up to 12 months at elevated temperatures indicate that preparation 06/142 is sufficiently stable to serve as a WHO reference reagent. In 2008, on the basis of the results of this study (WHO/BS/08.2083), preparation 06/142 has been established as the WHO reference preparation for pertussis antiserum (Human) for characterisation of assay systems.

2. CAUTION

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

The preparation contains material of human origin, and either the final product or the source materials, from which it is derived, have been tested and found negative for HBsAg, anti-HIV and HCV RNA. 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

Based on comparison of the antibody activity of preparation 06/142 in terms of the First International Standard (06/140) and the relevant US reference lot, each ampoule of preparation 06/142 contains anti-PT IgG content of 106 IU and IgA content of 18 IU; anti-FHA IgG content of 122 IU and IgA content of 86 IU; anti-69K IgG content of 39 IU and IgA content of 38 IU.

4. CONTENTS

Country of origin of biological material: Germany.
Each ampoule contains the residue of 1ml of pooled re-calcified human serum freeze dried on a five day cycle (starting shelf temperature -50°C) followed by back filling with high purity nitrogen before sealing. The ampoules contain no bacteriostat and the preparation should not be assumed as sterile.

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.
The entire contents of each ampoule of the 1st RR Pertussis Antiserum (human) should be completely reconstituted in 1 ml of sterile distilled water.

Form the collaborative study, an initial dilution at 1/100 - 1/200 of this solution for IgG assay is suggested. However, this may vary with individual laboratories.

In-house experiences indicate that aliquots of the reconstituted reference reagent could be used if they have been suitably stored at -20°C or -70°C. Since storage conditions can differ in individual laboratory, it is recommended that laboratories should carry out validation under their own storage conditions. Repeated freeze-thaw cycles of reconstituted antiserum should be avoided.

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. . 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.

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

9. REFERENCES

1) Collaborative Study Report: Dorothy Xing, Carl Heinz Wirsing von König, Penny Newland, Marion Riffelmann, Bruce Meade, Michael Corbel and Rose Gaines-Das "International collaborative study: Evaluation of proposed International Standard for pertussis antiserum (human)" WHO/BS/08.2083

2) Corbel MJ, Kreeftenberg JG and Knezevic I. WHO working group on the standardization and control of pertussis vaccines - report of a meeting held 6-7 May, Ferney Voltaire, France. Vaccine 22 (2004) : 293-300

3) Meade BD, Deforest A, Edwards KM, Romani TA, Lynn F, O'Brien CH, Swartz CB, Reed GF, and Deloria MA. Description and evaluation of serologic assay used in a multicenter trial of acellular pertussis vaccine. Pediatrics 1995,96:570-575

10. ACKNOWLEDGEMENTS

We gratefully acknowledge Dr Carl Heinz Wirsing von König, Institut für Infektiologie Krefeld GmbH (IIK), Krefeld, Germany for donation of the sera. Grateful acknowledgements are due to the Center for Biologics Evaluation and Research, FDA, Rockville, MD, USA for provision of ampoules of US Standard Pertussis Antiserum, Human, Lots 3, 4 & 5 included in the collaborative study. We would like to express our thanks to Dr Paul Matejtschuk (NIBSC) for assistance in the determination of freeze-drying conditions and for moisture and oxygen determinations for the ampouled material, and staff of CBRM for assistance with the filling procedure. We also thank all of the participants for their helpful contributions to the study.

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WHO International Laboratory for Biological Standards,
UK Official Medicines Control Laboratory

World Health Organization

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

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:	No	Irritant:	No
Flammable:	No	Handling:	See caution, Section 2
Other (specify):	Contains Material of Human 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 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: 1.0 - 2.0 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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