Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
Purified Protein Derivative (PPD) of Mycobacterium Avium Tuberculin
NIBSC code: PPDA
Instructions for use
(Version 5.0, Dated 19/10/2007)

1. INTENDED USE

This is the 1st International standard for PPD of Mycobacterium Avium Tuberculin and was established in 1954. It was prepared from a M. avium strain called D4. This material has been prepared and characterised by the Statens Serum Institut (SSI), Copenhagen, Denmark. The package insert from SSI is attached as page 3 - 4. This material is intended to be used in the potency assay of M. avium tuberculin preparations.

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

Each ampoule contains 500 000 International Units (IU) of PPD of M. avium Tuberculin.

4. CONTENTS

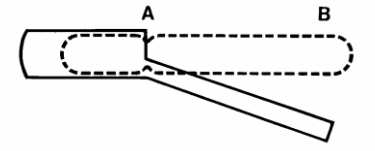
Country of origin of biological material: Denmark.
Each ampoule contains 10 mg PPD powder and phosphate salts. by definition each ampoule contains 500 000 IU of PPD of M. avium Tuberculin.

5. STORAGE

For long-term storage, this material should be stored at -20ºC.
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
The entire contents of each ampoule should be completely dissolved in an accurately measured amount of appropriate solvent (distilled water, saline or buffer) and the solution kept cool (e.g. 4ºC) prior to use. It is recommended that the solution is used immediately or aliquots should be stored at -20ºC. The ampoules contain no bacteriostat and the preparations should not be assumed to be sterile.

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

See Section 5 of SSI insert.

10. ACKNOWLEDGEMENTS

SSI, WHO

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 mycobacterial origin	

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

World Health Organization

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: 10 mg
Toxicity Statement: Toxicity not assessed
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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STATENS
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prevention and control of infectious diseases and congenital disorders

THE INTERNATIONAL STANDARD
for
PURIFIED PROTEIN DERIVATIVE (PPD) OF M. AVIAN TUBERCULIN
(1st international standard preparation)

1. THE STANDARD PREPARATION

The standard preparation was established in 1954[1]. It is prepared from a Mycobacterium avium strain called D4, which was grown on Dorset's synthetic medium. Purification was made by trichloracetic acid precipitation. Recently the name of this standard and the IU was slightly changed. The expression "Avium Tuberculin" was replaced by "M. avium Tuberculin"[2].

2. AMPOULE CONTENTS

A solution containing 4 mg/ml PPD in M/30 phosphate buffer at pH 7.0 was heated at 80°C on three successive days, distributed into ampoules (2.5 ml/ampoule), freeze-dried and ampoules were sealed under vacuum. Each ampoule therefore contains 10 mg PPD powder and phosphate salts. By definition [1], the total contents of each ampoule contains 500.000 International Units (IU) of Purified Protein Derivative (PPD) of M. Avium Tuberculin.

3. USE OF THE STANDARD

The standard preparation defines the International Unit (IU) and is intended to be used in the potency assay of M. avium tuberculin preparations. This, however, is not without complications and for a discussion of these and for a description of a recommended procedure for calibration of a local reference preparation, reference is made to the WHO Requirements for Tuberculins[3].

4. GENERAL REMARKS ABOUT INTERNATIONAL REFERENCE MATERIALS

International biological standards and international biological reference reagents provide a means of ensuring uniformity throughout the world in the designation of the potency of preparations used in the prophylaxis, therapy, or diagnosis of disease, where the potency cannot be expressed in terms of physical or chemical quantities. The International Units are units of quantities of "effective constituent"[4].

The standard is the material as it exists in the ampoules; the "material" thus includes the effective constituents together with all the other constituents that may be present (moisture, carrier, buffer, salt etc., according to the form in which the standard is available).

International biological reference materials are intended for use in the calibration of the contents of "effective constituent" in national or working standard preparations and for the expression of these contents in the respective International Units. For the routine use in the laboratory the national or working standards should be used in order to save as much as possible the international reference materials. These are only sent to individual laboratories in very limited amounts. The preparations are sent free of charges but sometimes a small charge might be claimed for the air-freighting.

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5. REFERENCES

1. WHO Techn. Rep Series No. 96, 1955, 11

2. WHO Techn. Rep. Series No (in press)

3. WHO Techn. Rep. Series No. 745, 1987, p.31 (Annex 1

4 N.K. Jerne & E.C. Wood, "The Validity and Meaning of the Results of Biological Assays", Biometrics 5, 273-299 (1949)

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