Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
House Dust Mite (Dermatophagoides pteronyssinus) Extract
1st International Standard 1984
NIBSC code: 82/518
Instructions for use
(Version 4.0, Dated 03/04/2008)

1. INTENDED USE

The 1st International Standard for House Dust Mite (*Dermatophagoides pteronyssinus*) extract consists of ampoules, coded 82/518, containing the freeze-dried residue of 1ml aliquots of an extract of *Dermatophagoides pteronyssinus* mite. This preparation was established as the 1st International Standard for House Dust Mite (*Dermatophagoides pteronyssinus*) Extract by the Expert Committee on Biological Standardisation of the World Health Organisation in 1984.

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

A potency of 100,000 International Units has been assigned to each ampoule.

4. CONTENTS

Country of origin of biological material: United Kingdom.
The bulk material for the 1st International Standard for House Dust Mite (Dermatophagoides pteronyssinus) extract consisted of a freeze-dried extract prepared from mites and the spent culture medium of human dander and yeast in aqueous buffer. The extract was centrifuged, filtered, dialysed against 0.005M ammonium bicarbonate buffer, again filtered and freeze-dried in volumes of 45mls. It was supplied to the National Institute for Biological Standards and Control (NIBSC) in this state and it was stored at –20°C prior to filling.

The bulk freeze-dried material was dissolved in sterile water at 1mg dry weight per ml giving a protein concentration of 0.3mg.ml-1 by the Lowry et al method[5]. It was then refiltered ending with a 0.2 micrometre membrane, homogenised by stirring and distributed into 4000 ampoules at 4°C. The mean weight of liquid contents of 74 checkweight ampoules taken at intervals during the fill was 1.0026 ± 0.29%. The contents of the ampoules were then freeze dried under the conditions normally used for international biological standards[6]. The mean moisture content based on dry weight of 1mg per ampoule was 1.013% (n=6).

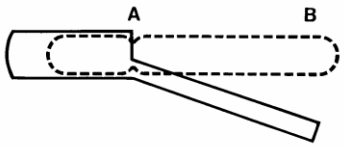
The 1st International Standard was selected from samples of candidate materials in a preliminary study[1] and was assessed together with two other freeze-dried preparations of (*D. pteronyssinus*) mite extract and a further liquid skin testing solution in glycerol saline in an international collaborative study involving 19 laboratories in 11 countries[2]. Examination of the activity of these preparations was by RAST inhibition, quantitative immunoelectrophoresis (CIE/CRIE and rockets), isoelectric focusing, quantitative skin testing, histamine release and other methods. The proposed standard was found to have biological activity and to be suitable for use as a standard. The following antigens were identified: *Der p* I (P1), *Der p* II (AgX), Dp Y and Dp 23. The content of *Der p* I in the standard was estimated to be between 10 –31 micrograms per ampoule by laboratories participating in the collaborative study. Each ampoule was assigned 100,000 international units of potency. Later reports state that the standard contains 12.5 micrograms of Der p I and 0.4 micrograms of *Der p* II [3-4].

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

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 total contents of the ampoule should be reconstituted with 0.5ml distilled water and dissolved gently by swirling to avoid froth. The reconstituted reagent should be used as soon as possible after reconstitution

8. STABILITY

Accelerated degradation studies have shown that the 1st International Standard is very stable in unopened ampoules stored at –20°C. The predicted loss of activity is <0.001% of the original potency per year when stored at that temperature.
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

1. Ford, A.W., Rawle, F.C., Lind, P., Spieksma, F.T.M., Lowenstein, H. & Platts-Mills, T.A.E. Standardisation of *Dermatophagoides pteronyssinus*: assessment of potency and allergen content in ten coded extracts. Int. Arch. Allergy Appl. Immunol. **76**: 58-67 (1985)

2. Ford, A.W., Seagrott, V., Platts-Mills, T.A.E. & Lowenstein, H. A collaborative study on the first international standard of *Dermatophagoides pteronyssinus* (house dust mite) extract. J. Allergy Cllin. Immunol. **76:** 676-686 (1985)

3. W.H.O. Dust mite allergens and asthma: a worldwide problem. Bull. WHO **66**: 769-780 (1988).

4. International Workshop Report: Dust mite allergens and asthma: worldwide problem. J. Allergy Clin. Immunol. **83**: 416-427 (1989).

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

5. Lowry, O.H., Rosebrough, N.J., Farr, A.L., & Randall, R.J. Protein measurement with the folin phenol reagent. J. Biol. Chem. **193**: 265-275 (1951).

6. Campbell, P.J., International Biological Standards and Reference Preparations. II. Procedures used for the production of biological standards and reference preparations. J. Biol. Stand. **2**: 259-267 (197).

10. ACKNOWLEDGEMENTS

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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 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: 0.01g
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.