Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
Birch (Betula verrucosa) Pollen Extract
NIBSC code: 84/522
Instructions for use
(Version 5.0, Dated 24/07/2013)

1. INTENDED USE

The first International Standard for Birch (*Betula verrucosa*) pollen extract consists of ampoules, coded 84/522, containing the freeze dried residue of 1ml aliquots of an extract of Birch Pollen. This preparation was established as the 1st International Standard for Birch (*Betula verrucosa*) pollen extract by the Expert Committee on Biological Standardisation of the World Health Organisation in 1986.

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

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

4. CONTENTS

Country of origin of biological material: United Kingdom.
The first International Standard for Birch *(Betula verrucosa)* pollen extract consists of a freeze-dried extract prepared from a mixture of Birch pollen from 3 different years of collection. The pollen was more than 95% pure Birch pollen and there was less than 5% non-pollen particles by microscopic count. The pollen was defatted in diethyl ether and extracted in a solution containing sodium bicarbonate 0.6% (w/v), sodium chloride 0.5% (w/v) and thimerosal 0.020% (w/v). The extract was filtered, dialysed and freeze-dried. A total of 12.5g of freeze-dried material was supplied to the National Institute for Biological Standards and Control (NIBSC).

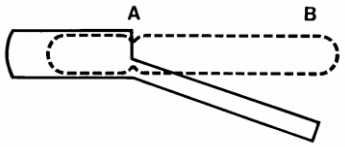
At NIBSC the bulk freeze-dried material was dissolved in sterile distilled water at approximately 3mg dry weight per ml. It was then re-filtered ending with a membrane of pore size 0.22µm and distributed in 1ml volumes at room temperature into 3,500 ampoules, coded 84/522. The mean weight of liquid content of 79 checkweight ampoules taken at intervals during the fill was 1,00266gm ± 0.13%. The contents of the ampoules were then freeze-dried and secondarily desiccated under the conditions normally used for international biological standards. The mean dry weight was 3.53mg (n=6) and the moisture content was 0.46% (n=6).

5. STORAGE

Store unopened ampoules 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 lml of distilled water and dissolved by gently swirling to avoid froth. No attempt should be made to weigh out any portion of the freeze- dried material. The reconstituted standard should be used as soon as possible after reconstitution and no attempt should be made to store it in the reconstituted state
Biological Activity.

The 1st International Standard was assessed together with 4 other freeze-dried preparations of birch pollen extract in an international collaborative study involving 20 laboratories in 11 countries[(l)]. 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 only major and dominating allergen in birch pollen extract, *Bet v* I (Ag23), was identified. The relative contents of this allergen corresponded with the relative total activities of the standard and the other extracts studied. Other antigens identified and assayed in the preliminary study were Ag19 and Ag25. Each ampoule was assigned 100,000 International Units of potency.

8. STABILITY

Accelerated degradation studies have shown that the 1st International Standard is very stable in unopened ampoules at – 20°C. The predicted loss of activity is approximately 0.02% 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

None

10. ACKNOWLEDGEMENTS

All participants in the collaborative study.
We would like to express our gratitude to the following, who by provision of finance, and in some cases also of extracts, made this work possible: Abello, Madrid, Spain; Allergopharma, Hamburg, Germany; Allermed, San Diego, Calif. USA; Allergy Laboratories of Ohio, Colombus Ohio, USA; Allergy Laboratories, Oklahoma City, Okla. USA; ALK Laboratories, Copenhagen, Denmark; Antigen Laboratories, Liberty, Mo. USA; Beecham, Betchworth, Surrey, UK; Berkeley Biologicals, Berkeley, Calif. USA; Center Laboratories, Port Washington, N.Y, USA; Diephuis Pharmacia, Groningen, The Netherlands; Greer Laboratories, Lenoir, N.C, USA; HAL Allergenen Laboratories, Haarlem, The Netherlands; Hollister-Steir, Spokane, Wash., USA; Laboratories Hamon, Montreal, Canada; Lofarma, Milano, Italy; Meridian Bio-Medical, Denver, USA; NYCO, Oslo, Norway; Omega Laboratories, Montreal, Canada; Pharmacia, Uppsala, Sweden and Stallergenes Laboratories, Paris, France.

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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 biological 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.